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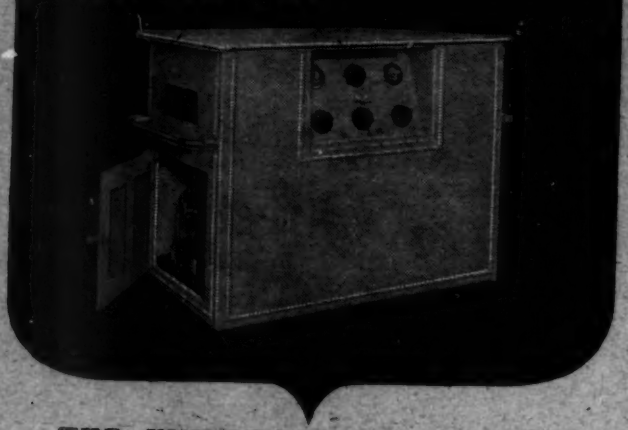

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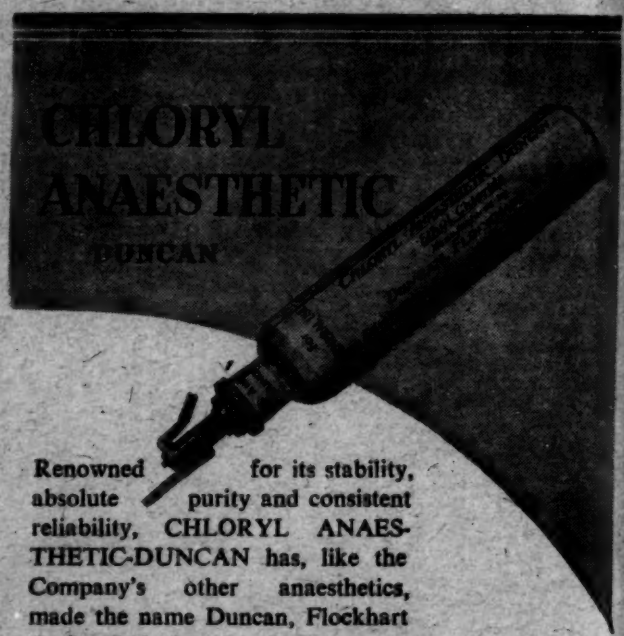

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BRITISH MEDICAL JOURNAL

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FAT METABOLISM AND THE SPRUE SYNDROME*

BY

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The sprue syndrome is characterized by a defect of fat absorption, commonly associated with diarrhoea, wasting, abdominal distension, the radiographic segmentation pattern of the small intestine, absence of the normal post-absorptive systemic hyperlipaemia, a flattened oral glucose-tolerance curve, anaemia, and certain vitamin deficiencies. Defective fat absorption may be regarded as an essential part of the sprue system by definition. The sprue syndrome may be taken to include non-tropical sprue (idiopathic steatorrhoea) (Thaysen, 1932), tropical sprue (Fairley, 1936), and the coeliac syndrome in children (Parsons, 1932). To these may perhaps be added some cases of gastro-colic fistula. Other cases of defective fat absorption (such as the post-gastrectomy syndrome, regional ileitis, chronic pancreatitis, or obstructive jaundice) are not usually associated with a sufficient number of the characteristic features of the sprue syndrome to warrant their inclusion in this group (see Table I).

Tropical sprue can occur in epidemic outbreaks involving groups of people living under similar environmental conditions—this was often observed during the last war in South-east Asia—non-tropical sprue and the coeliac syndrome, however, occur more or less sporadically, although several cases may occur in one family. With tropical sprue recovery is the rule; with non-tropical sprue and the coeliac syndrome complete recovery is relatively rare. The syndrome in its more chronic form can be divided into two main parts—a more or less constant group of signs and symptoms, including the fat-absorption defect, and a more variable element, subject to exacerbations from time to time, including severe diarrhoea with bulky fermenting stools, vitamin-B deficiencies, and haematological changes.

TABLE I.—*Features of the Sprue Syndrome*

	Coeliac Syndrome	Non-tropical Sprue	Tropical Sprue	Gastro-colic Fistula	Post-gastrectomy Syndrome	Regional Ileitis	Obstructive Jaundice	Chronic Pancreatitis
Fat-absorption defect	+++	+++	+++	++	++	++	+++	+++
Proportionate defect	+++	+++	+++	?	—	—	—	?
Flat chylomicrograph	+++	+++	+++	++	—	—	(+++)	(+++)
Fine intraluminar emulsification	+++	+++	+++	+++	?	+++	—	—
Radiographic "deficiency pattern"	+++	+++	+++	++	—	—	—	?
Flat oral glucose curve	++	++	++	—	—	—	?	—
Macrocytic anaemia	—	+++	+++	+++	+	+	+	+?
Microcytic anaemia	+++	+	—	—	—	—	—	—
Iron deficiency	+++	+++	+++	?	—	—	?	—
Tetany: Low serum calcium	++	++	—	—	—	—	—	—
Low serum phospholipid	+++	+++	+++	?	—	—	++	++
Low serum cholesterol	+++	+++	+++	?	—	—	++	++
Signs of vitamin-B deficiencies	++	++	++	++	++	+	—	+

+++ Usually present. ++ Commonly present. + May be present. — Usually not present.

Certain differences can be observed between non-tropical and tropical sprue and the coeliac syndrome. The anaemia in the coeliac syndrome is usually microcytic, probably due to iron deficiency; an iron-deficient component is also commonly observed in the adult macrocytic anaemia. There may be several primary aetiological factors which can give rise to the sprue syndrome, and it is probable that different factors are operative in the three varieties of the syndrome under consideration.

*Read in opening a discussion at a joint meeting of the Sections of Pathology and Bacteriology and of Tropical Medicine at the Annual Meeting of the British Medical Association, Harrogate, 1949.

The Fat-absorption Defect in the Sprue Syndrome

1. Normal Fat Absorption in Man

Absorption from the intestine is conveniently considered in three phases: an intraluminar, a cellular, and a distributive phase. The absorption of fat must be studied both from a general point of view and in detail (Frazer, 1947a).

General Aspects of Fat Absorption.—The quantity of fat absorbed must be determined by the use of a fat-balance technique (Cooke *et al.*, 1946). More recently the method of de Kamer, Huinick, and Weyers (1949) has been successfully used. The criticisms of Annegers, Boutwell, and Ivy (1948) are not valid with regard to the use of these balance techniques for studies of defective fat absorption. The amount of fat ingested may be increased from 50 to 100 g. and the effect of this fat-loading of the diet determined quantitatively. The effect of different types of dietary fat can also be studied. In

addition to quantitative measurements, the characteristics of the faecal fat and the quantity of volatile short-chain fatty acids can also be determined. The results of observations made by these various methods in normal subjects are shown in Table II.

TABLE II.—*General Study of Fat Absorption*

	Normal	Sprue Syndrome
Fat-balance technique 5–12 day balance .. Daily fatty acid (de Kamer, 1949).. ..	> 95%	50–80%
Fat-loading tests 50 to 100 g.	Proportionate, 48–95 g.	Proportionate, 35–70 g.
Fat-assimilation test ..	Natural fats absorbed	Intolerance of saturated fats
Faecal fats	< 3 g. in 24 hr.	Neutral fat and fatty acid +++; 10–50 g. in 24 hr. High M.Wt. and M.P., low I.V.
	< 2 g. per 100 g. dried faeces	Volatile fatty acid +++ up to 8 g. per 100 g. dried faeces

Detailed Study of Fat Absorption.—The intraluminar phase of fat absorption can be studied by an intestinal intubation technique (Thompson, 1949). A Miller–Abbott tube is passed into the small intestine and samples of intestinal contents taken before and after the administration of fat. The material recovered is examined for the presence or absence of enzymes and other substances and the changes which the fat has undergone. The action of enzymes, the effect of added bile, and the presence of bacteria can also be investigated. The cellular phase can be studied only indirectly in man, and at present interpretation is difficult. Investigation of the distributive phase is confined to blood-fat studies. The results in normal subjects are shown in Table III.

TABLE III.—*Detailed Study of Fat Absorption*

	Normal	Sprue Syndome
Intraluminar phase: intubation technique		
Hydrolysis	10% or more	10% or more
Emulsification	Particle diameter < 0·5 μ	Apparently normal
Bile addition	Enhances lipolysis only in resting samples	Enhances lipolysis in all samples
Enzymes	Lipase, trypsin, amylase, and lysozyme present. Lecithinase absent	Lipase, trypsin, and amylase present. Lysozyme? and lecithinase absent
Bacteria	Absent, or small numbers only	Present in upper intestine in large numbers
Cellular phase:		
Blood biochemistry		
Phospholipid ..	About 250 mg./100 ml.	Low. 40–200 mg. (average 142 mg. in 60 estimations)
Cholesterol	About 250 mg./100 ml.	Low < 150 mg./100 ml.
Particulate absorption ..	Present	*No* systemic hyperlipaemia
Other absorption tests ..	Normal tolerance curve	Oral glucose-tolerance curve flattened
Effect of therapy ..	Nothing conclusive	
Distributive phase:		
Chylomicrographs ..	Normal peak 150 particles per field	Flat
Blood-fat curves	Normal peak 200 mg./100 ml. blood	,,

2. Fat Absorption in the Sprue Syndrome

The changes observed when using these methods for the study of fat absorption in the sprue syndrome are shown in Tables II and III.

General Aspects.—In the general study of fat absorption the characteristic changes in the sprue syndrome consisted of a fat-absorption defect, only 50–70% being absorbed. The fat-loading tests show that the defect was proportionate to the amount ingested. Thus, if 50 g. were administered and 35 g. absorbed, the administration of 100 g. resulted in the absorption of 70 g. or more. With regard to fat assimilation, fats containing a large quantity of long-chain saturated fatty acids were less well tolerated by sprue patients than by normal individuals. Patients suffering from the sprue syndrome tolerated milk and milk products better than mutton fat or beef fat. The faeces contained abnormal amounts of long-chain fatty acids up to 30 g. or more in 24 hours. The neutral fat was usually about 80% hydrolysed, and the fatty acids were often present as crystals and can be shown to have a high melting point, high molecular weight, and low iodine value (Parsons, 1932; de Kamer, 1949). Volatile short-chain fatty acids were often present in large quantities.

Detailed Study.—The detailed study of fat absorption showed differences from normal. Hydrolysis and initial emulsification in the upper part of the small intestine seemed to be within normal limits. Small but significant changes in emulsification may not be detected by this method; clear differences were found in cases of obstructive jaundice or chronic pancreatitis, in which emulsification was grossly defective. The addition of bile caused enhancement of lipolysis in all samples. The reason for this difference from normal is obscure. All the usual enzymes were present in approximately normal concentration, with the possible exception of lysozyme. Bacteria were present in large numbers in the upper intestine, especially in achlorhydric patients. The bacteria found were intestinal flora, which are normally confined to the lower part of the intestine.

With regard to the cellular and distributive phases, low blood phospholipid and cholesterol were usual. The oral glucose-tolerance curve was commonly depressed. There was no post-absorptive systemic hyperlipaemia following fat absorption, as shown by chylomicrographs and blood-fat curves.

Discussion

It is difficult to study the cellular phase of fat absorption in the human subject except by indirect methods. It is agreed by all workers that long-chain triglycerides can be observed as particles in the intestinal cell during absorption, and that these particles pass from the cell through the corium of the villus to the lacteal, and thence by the lymphatic route into the blood stream, giving rise to the normal post-absorptive systemic hyperlipaemia. There is evidence to support the view that these particles pass unhydrolysed, or partly hydrolysed, into the cell from the intestinal lumen, and that adequate emulsification, normal electrolyte absorption, and possibly phospholipid synthesis may influence this stage of particulate absorption (Frazer, 1948).

Alternatively, the triglycerides are resynthesized from fatty acids and glycerol inside the intestinal cell. The post-absorptive systemic hyperlipaemia is dependent upon normal particulate absorption. Absence of the normal hyperlipaemia might be due to interference either in the intraluminar or in the cellular phase, according to the partition theory (Frazer, 1946), but according to the lipolytic hypothesis (Verzar and McDougall, 1936) it must be due to faulty resynthesis in the cell. The effect of added lipase on the post-absorptive hyperlipaemia and the normal intestinal radiographic pattern during fat absorption in human subjects support the experimental evidence in animals upon which the partition theory is based. From either point of view, however, the absence of the post-absorptive systemic hyperlipaemia must be interpreted as evidence of defective absorption of triglycerides in particulate form.

It is concluded from the evidence presented that there is interference with particulate absorption in the sprue syndrome, and that larger quantities than normal of fatty acid are both absorbed and excreted. It is not possible at present to determine with certainty whether the interference with particulate absorption occurs in the intraluminar or in the cellular phase. The more unsaturated long-chain fatty acids appear to be absorbed, while the more saturated are excreted. This would account for the proportionate nature of the defect and for a number of secondary changes which will now be considered in detail.

The Effects of the Fat-absorption Defect in the Sprue Syndrome

Intestinal Mucin.—As a result of faulty particulate absorption, greater quantities of long-chain fatty acids occur in the intestinal lumen. Administration of long-chain fatty acids resulted in an increase of mucus in the intestinal lumen in normal human subjects and experimental animals, unsaturated fatty acids being more effective than saturated fatty acids. Mucus is an activator of lipolysis in the presence of bile salts. The administration of long-chain or short-chain fatty acids or hypertonic solutions induced the so-called radiographic "deficiency pattern" in normal human subjects. The changes observed were radiographically indistinguishable from those found in the sprue syndrome. The segmentation of the barium sulphate suspension was shown to be due to flocculation in the presence of mucus. The relative proportions of mucus to barium sulphate suspension were important (Frazer, French, and Thompson, 1949). There is little doubt that more mucin is present in the small intestine in a case of sprue than in a normal individual. Whether this is due to oversecretion, or whether lack of destruction of mucin may also be concerned, has not yet been determined. An increased quantity of long-chain fatty acids is at least partly responsible for the presence of excessive quantities of mucus.

Faecal Fat.—The amount of faecal fat was increased and the output of long-chain saturated fatty acids seemed to be selective and sometimes closely associated with mucin. Long-chain saturated fatty acids are not well absorbed by normal animals. The failure to absorb these fatty acids in sprue would account for the fact that the defect is proportionate and for the observation that sprue patients do not tolerate triglycerides containing much saturated fatty acid. The more unsaturated fatty acids are presumably absorbed, and, in accordance with observations in animals, they must be transported by an alternative route to the thoracic duct and thus do not give rise to a systemic hyperlipaemia. Long-chain fatty acids may cause irritation and diarrhoea, which can be controlled by the administration of calcium salts, which precipitate the long-chain fatty acids as insoluble soap. Excessive fatty acid formation might under certain circumstances be responsible for inadequate absorption of calcium and iron. The absorption of both calcium and iron is a complex question, however, and it is unlikely that any single factor accounts for their poor assimilation in the sprue syndrome.

Hypochlorhydria.—Administration of long-chain fatty acids will cause a decrease in gastric motility and gastric secretion, particularly certain long-chain unsaturated fatty acids. In the sprue syndrome decrease of gastric motility and acidity is marked. Hypochlorhydria is usual; achlorhydria may occur. The hypochlorhydria observed in sprue may be due to the absorption of abnormal quantities of long-chain fatty acids. Hypochlorhydria and large quantities of mucin in the intestinal lumen cause a relative fixation of *p*H, which, with decreased gastric and intestinal motility and interference with absorption, help to provide suitable conditions for increased growth of bacteria. Many intestinal bacteria can split triglycerides and may help in the hydrolysis of neutral fat to fatty acid, and they may also ferment starch. Starch fermentation may be pronounced in the sprue syndrome, giving rise to volatile short-chain fatty acids (acetic, propionic, and butyric) in large quantities in the faeces. These acids may be irritant to the intestine, giving rise to diarrhoea, which is not readily stopped by the administration of calcium salts.

Blood Biochemistry.—Certain changes in blood biochemistry were usually seen, particularly a decrease of phospholipid and of cholesterol in the blood. These changes might be due either to faulty absorption or to faulty synthesis. Particulate absorption may be closely related to absorption of phospholipid and to its synthesis in the intestinal cell. Cholesterol was also found to be associated with particulate fat in the chyle. However, the quantities involved were small and no close relation between blood phospholipid, cholesterol, and triglyceride was demonstrable during fat absorption (Frazer and Stewart, 1937). It seems likely, therefore, that the changes in blood phospholipid and cholesterol in sprue may also be related to decreased synthesis of these substances in the liver or elsewhere. There is no clear evidence at present to determine whether interference with synthesis or faulty absorption is the more important factor. Large quantities of long-chain fatty acids passing direct to the liver might modify liver function.

Discussion

The probable interrelationship of these various effects of abnormal fat absorption in the sprue syndrome is indicated in Fig. 1. Faulty particulate absorption of unhydrolysed

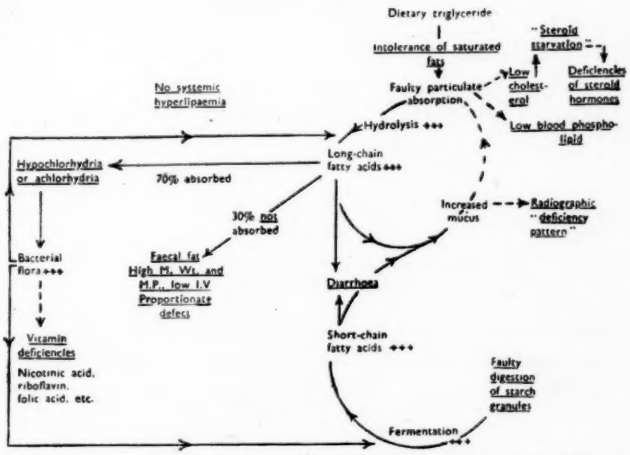

FIG. 1.—Fat-absorption defect in sprue syndrome. Continuous lines indicate points which have been demonstrated experimentally.

fat results in increased hydrolysis; the long-chain fatty acids formed are partly absorbed, causing increased mucus in the intestinal lumen; it is suggested that the excess mucus in the intestinal lumen may interfere with particulate absorption. The long-chain saturated fatty acids are not absorbed and passed out in the faeces. By taking this as the basic fault in the fat-absorption mechanism the main features of the sprue syndrome are readily explained. Thus the composition of dietary triglyceride, especially with regard to its saturated fatty acid content, will affect the sprue patient.

The absence of the systemic hyperlipaemia, although 70% of the fat is absorbed, the proportionate nature of the defect, and the occurrence of hypochlorhydria are explained on the basis of fatty acid absorption (Frazer, 1943). The failure to absorb the more saturated fatty acids is clearly shown by their appearance in the faeces. The existence of diarrhoea, which is only sometimes controlled by calcium, is due to the fact that it can be caused by long-chain fatty acids derived from fat breakdown or by short-chain fatty acids arising from starch fermentation.

The radiographic "deficiency pattern" has been shown to be due to flocculation of the barium sulphate suspension

with mucus. The changes in cholesterol and phospholipids may follow from failure of particulate absorption, or, alternatively, may be due to the effect of excessive amounts of long-chain fatty acids on liver function. Changes in steroid hormones and bile phospholipid may be secondary to the changes in blood cholesterol and phospholipid respectively. Symptoms can be aggravated in many cases of the coeliac syndrome by increasing the dietary starch (Parsons, 1932).

Relation of Fat-absorption Defect in the Sprue Syndrome to Multiple Aetiological Factors

The relation of the fat-absorption defect in the sprue syndrome to possible aetiological factors is shown in Fig. 2.

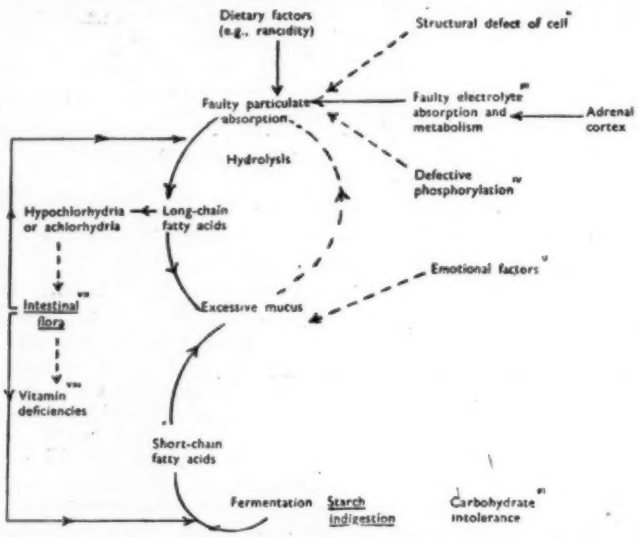

FIG. 2.—Fat-absorption defect in sprue syndrome in relation to aetiological factors.

Eight main causative factors of the sprue syndrome have been suggested, each of which will be considered briefly.

1. *Dietary Factors.*—The more saturated fats aggravate the fat-absorption defect. Special characteristics of the dietary fat, such as oxidative rancidity, may play some part in the aetiology of tropical sprue, especially when it occurs in groups of individuals under similar environmental conditions. Stannus (1942) suggested that dietary factors might have some causative role in tropical sprue. The inclusion of rancid fats in the diet causes diarrhoea, anaemia, and destruction of dietary vitamins (Whipple, 1932; Burr and Barnes, 1943; Györgi *et al.*, 1942). The possible significance of rancid dietary fats in the onset of tropical sprue in India was noted by J. M. French. It is unlikely that rancidity is a major aetiological factor in non-tropical sprue or in the coeliac syndrome in this country. Diarrhoea has been recently observed in infants in temperate climates receiving rancid cod-liver oil (Whipple, 1936). Rancid fats are readily hydrolysed, and the fatty acids liberated are irritant and are effective stimulants of mucus secretion. The effects of dietary fats and the products of rancidity on the fat-absorption mechanism are being investigated. Dietary factors may have some importance in the aetiology of tropical sprue.

2. *Structural Defect of the Intestinal Cell.*—It was suggested by Hurst (1941) that structural defects of the intestinal muscularis mucosa might be responsible for the fat-absorption defect in the sprue syndrome. Atrophic changes of the intestinal wall are not uncommon at necropsy. It is improbable that these changes are present in the many cases of tropical sprue which make a complete recovery. Secondary structural changes might perpetuate faulty particulate absorption and represent an irreversible stage of defective fat absorption in sprue cases of long standing.

3. *Disturbances of Electrolyte Metabolism (Adrenal Cortical Insufficiency).*—Adrenal cortical deficiency has been suggested as a primary aetiological factor in sprue (Verzar and Laszt, 1935), since it was thought to be necessary for phosphorylation and resynthesis of triglycerides. It has been established subsequently that the adrenal cortex does not affect phosphorylation in the intestine (Stillman, Entenman, Anderson, and Chaikoff, 1942). Low blood sodium and hypotension are not uncommon in sprue, although usually observed in severe rather than early cases (Black, 1946). Changes in electrolyte metabolism and absorption might interfere with the particulate absorption of triglycerides (Frazer, 1949). In the sprue syndrome, however, treatment with adrenal cortical hormone, corticotropin, and other measures which brought the blood sodium back to normal levels did not markedly affect the fat-absorption defect. Cases of Addison's disease may show a defect of fat absorption, but they do not develop the sprue syndrome. A low level of free cholesterol in the blood may possibly result in a generalized steroid starvation, resulting in secondary hormone deficiencies, such as adrenal cortical insufficiency and delayed sexual development. Water and electrolyte changes may contribute to the fatal termination in severe cases of sprue, but they probably are not materially concerned in the primary aetiology of the sprue syndrome.

4. *Defective Phosphorylation (Adrenal Cortical Insufficiency—Verzar).*—There is little evidence of any direct relation between phosphorylation in the intestinal cell and triglyceride absorption. Simultaneous absorption of lecithin facilitates the absorption of long-chain triglyceride (Sagrott, 1949). The amount of phospholipid formed during fat absorption may be small, and for this reason phospholipid cannot be regarded as an obligatory intermediate in fat absorption (Zilversmit, Entenman, and Chaikoff, 1948). Faulty phosphorylation of fat in the sprue syndrome has been largely assumed on the basis of flat oral glucose-tolerance curves which have been attributed to failure in the phosphorylation of carbohydrate (Verzar and McDougall, 1936; Maegraith *et al.*, 1945). Other experimental studies have not supported this interpretation of the sugar curves (Emery, 1947; Fourman, 1947). Apart from the low blood phospholipid commonly observed, there seems to be little evidence of faulty phosphorylation in the sprue syndrome. If it did occur, it might affect particulate absorption as indicated.

5. *Emotional Factors.*—These cannot be disregarded in a gastro-enterological syndrome. Movement and secretion may be affected: certain other psychosomatic disorders are associated with excessive mucous secretion. Such changes might precipitate the sprue syndrome; there is no direct evidence of the mechanism at the present time.

6. *Starch Fermentation.*—In cases of the coeliac syndrome the fat-absorption defect may be aggravated by the administration of starch. Carbohydrate intolerance in the coeliac syndrome is well known (Parsons, 1932). The primary defect seems to be faulty digestion of starch granules and consequent starch fermentation, giving rise to short-chain fatty acids. Intolerance of starch also occurs in many cases of adult sprue. An extensive investigation into the mechanism of starch granule digestion and its relation to mucinases and lysozyme is being undertaken. It is possible that starch fermentation may have an aetiological significance in some cases of the coeliac syndrome.

7. *Intestinal Flora.*—Changes in intestinal flora occur in the sprue syndrome, more affecting the site of growth than the type of organism present. The predominating bacteria may vary, however, owing to alteration in environmental conditions consequent upon faulty absorption or other changes. The higher level of intestinal flora, which may reach the upper small intestine in sprue, may give rise to successful competition of the bacteria with the host. This competition hypothesis of the common vitamin deficiencies in sprue will be more fully discussed in another communication. Changes in intestinal flora are probably secondary in tropical and non-tropical sprue and the coeliac syndrome. Intestinal bacteria can hydrolyse triglycerides and ferment starch. They could therefore initiate changes which might lead to the sprue syndrome. Such a mechanism might possibly be involved in some cases of gastrocolic fistula.

8. *Vitamin Deficiencies.*—Deficiencies of riboflavin, nicotinic acid, and folic acid are fairly common in sprue—other vitamin

deficiencies are rather rare. It has been suggested that these vitamin deficiencies constitute a primary aetiological factor in the sprue syndrome (Verzar and McDougall, 1936; Castle, Rhoads, Lawson, and Payne, 1935). There is no satisfactory evidence of a direct relation between these vitamins and the fat-absorption mechanism (Frazer, 1947b). The signs of these deficiencies can be dramatically relieved without any effect on the fat-absorption defect (Cooke *et al.*, 1946). Classical cases of deficiency of these vitamins may occur with normal fat absorption. These deficiencies, which come and go during the course of the sprue syndrome, are probably secondary changes attributable to successful competition with the host for common essential nutrients on the part of intestinal bacteria.

Conclusions

It is concluded that the underlying fat-absorption fault is a defect in particulate absorption. The consequent absorption and excretion of fatty acids account for most of the major features of the sprue syndrome. Certain intermittent characteristics may be attributed to high growth of intestinal bacteria. The primary cause of faulty particulate absorption probably varies in different cases—many cases of tropical sprue may be primarily due to dietary faults, whereas some underlying defect, possibly an enzyme deficiency, may be a major factor in most cases of non-tropical sprue and the coeliac syndrome. Intestinal flora changes occur secondarily in most cases of sprue, but they may have a more important aetiological role in some cases of gastro-colic fistula. The final picture of the aetiology of the sprue syndrome will be achieved only as a result of further detailed study of the fat-absorption defect and experimental investigations designed to differentiate primary and secondary changes.

Much of the original work referred to in this paper is still in progress as part of the programme being undertaken in the Department of Pharmacology, University of Birmingham, by a team which includes Dr. J. M. French, Dr. M. D. Thompson, Dr. H. G. Sammons, Dr. R. Schneider, Dr. P. E. Sagrott, Mr. W. R. Pover, Mr. W. D. Brown, Mr. G. A. Rowe, and Mr. B. G. Taylor. While acknowledgments are made in the text to individual members with regard to points with which they have been especially concerned, the progress of the work is essentially dependent upon the combined efforts of the whole team. I am most grateful to many colleagues on the staff of the Birmingham United Hospital, especially to Professor T. L. Hardy, Dr. W. T. Cooke, Dr. A. L. Peeney, Dr. C. F. Hawkins, and Dr. Garfield Thomas, whose close collaboration and help have been invaluable. I am indebted to the Medical Research Council and the Sir Halley Stewart Trust for financial assistance in this work.

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THE TREATMENT OF MALIGNANT TERTIAN MALARIA*

BY

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The early diagnosis of malignant tertian malaria is a matter of the first importance, so that specific therapy may be started with the least possible delay. In recent years the development of modern methods of rapid transport has made it all the more imperative that medical men in all parts of the world should be familiar with the many diverse clinical manifestations of this disease.

My first experience of the difficulties which may be encountered in the diagnosis of *Plasmodium falciparum* infections occurred at an early stage of the 1914–18 war, when I was in charge of a wing of a military hospital in Nairobi. One morning about 80 British soldiers who had been evacuated from the vicinity of Lake Victoria Nyanza and sent down the line by hospital train were admitted under my care. A preliminary examination of these men disclosed a great variety of clinical symptoms, as the result of which I made a number of provisional diagnoses.

Many of the patients were obviously the victims of malaria, but there were others whose symptoms were unlike any which are usually associated with this disease. Several seemed to be suffering from some acute abdominal condition, such as appendicitis, pancreatitis, or biliary colic. Some were passing blood and mucus per rectum, and these I diagnosed as dysentery. Two or three had the clinical appearance of typhoid fever, and there were several with cerebral symptoms which I thought were probably due to heat-stroke. In one case I suspected amoebic hepatitis and in others bronchitis or bronchopneumonia. A blood smear was taken from each patient as a routine procedure and sent to the laboratory for examination; the presence of malignant tertian malaria parasites was reported in every single instance. The administration of quinine, at that time the only antimalarial drug available, was followed in all cases by prompt alleviation of symptoms and ultimate recovery.

My object in recounting this incident is to impress on those who are about to practise in malarious regions or to sail in ships which may touch at ports where the disease is endemic that malignant tertian infections often fail to conform to the popular conception of malarial fever. They may simulate a great variety of other diseases, and failure to recognize this fact has resulted in the loss of many lives which could have been saved by the prompt application of

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specific antimalaria treatment. In the past 12 months two striking examples illustrating this point have come to my notice.

Illustrative Cases

The first case was that of a young woman who visited the Victoria Falls in the course of a holiday tour in South Africa and fell ill with headache and a slight rise of temperature some 10 days later. She had no idea that she had been exposed to the risk of malarial infection, and treated herself for several days with aspirin and other non-specific drugs. Soon after reaching Johannesburg her condition suddenly became critical, and she was admitted to hospital suffering from cerebral malaria, as the result of which she died in spite of all efforts to save her life.

The other case was that of a stewardess employed in a ship on the outward run from London to Capetown. Her illness began in very much the same manner about 10 days after leaving the port of Beira, on the East African coast. Several of the crew were down with malaria, and owing to shortage of nursing staff she continued to attend to them for several days before reporting sick. When she did so, the ship's surgeon, who had had no previous experience of tropical diseases, made a provisional diagnosis of influenza and prescribed codeine. She was ultimately sent ashore at Capetown in a comatose condition and admitted to hospital. A blood smear revealed a very heavy infection with *P. falciparum*, and she was given immediate parenteral treatment with antimalarial drugs. This case fortunately ended in recovery, though during the first 24 hours after admission her condition was the cause of grave anxiety.

These two cases illustrate two characteristic features of malignant tertian malaria: (1) that the disease often has an insidious onset, and (2) that in the absence of specific treatment the patient may with little or no warning become critically ill with so-called "pernicious" symptoms, which have been variously classified as cerebral, algid, bilious, remittent, pneumonic, and cardiac. More often than not the paroxysm is ill defined and rigors are exceptional, the temperature rarely exceeding 104° F. (40° C.). A double peak in the temperature chart owing to the segmentation of two groups of parasites is common, and there may be three, four, or more groups, each segmenting independently and giving rise to continuous fever, with several peaks in the 24 hours.

It is important also to recognize that in a primary case parasites may be so scanty in the peripheral blood during the first few days of fever that they may not be detectable in a blood smear, even if no antimalarial drug has been administered. A negative smear, particularly if this has been taken at the height of the fever, should not therefore be regarded as excluding the possibility of malarial infection. The wisest course in such cases is to administer an antimalarial drug and to take another blood smear immediately the temperature drops, when it is often possible to confirm the diagnosis.

Mode of Action of Antimalarial Drugs

It is necessary to consider this subject in relation to the various phases in the life-cycle of the malaria parasite in the human body. The recent demonstration by Shortt and his co-workers of an exo-erythrocytic phase of *Plasmodium cynomolgi* in the monkey and of *P. vivax* in man, and the subinoculation experiments of Fairley and his colleagues in Australia, have greatly clarified our knowledge of this problem, which had been for so many years a matter of speculation (Shortt and Garnham, 1948; Shortt, Garnham, Covell, and Shute, 1948; Fairley *et al.*, 1947).

Antimalarial drugs may act in four possible ways: (*a*) against the primary tissue, or pre-erythrocytic, phase of the parasite; (*b*) against the asexual parasites in their erythrocytic phase; (*c*) against the sexual parasites in their erythrocytic phase; and (*d*) against the hypothetical persistent tissue phase of the parasite, to which latency and late relapse in *vivax* malaria have been attributed (Shannon, 1948). There is convincing evidence against the existence of the last-named stage in *falciparum* infections, and only the first three categories are considered here (see Table).

Table Showing the Action of Various Drugs on P. falciparum

Class of Drug	Action on		
	Pre-erythrocytic Phase	Erythrocytic Phase (Asexual Forms)	Erythrocytic Phase (Sexual Forms)
Cinchona alkaloids (e.g., quinine)	−	+	−
9-aminoacridines (e.g., mepacrine)	−	+	−
4-aminoquinolines (e.g., chloroquine, camoquin)	−	+	−
8-aminoquinolines (e.g., pamaquin, pentaquine, isopentaquine)	+	−	+
Biguanides (e.g., proguanil) ..	+	+	−*
Sulphonamides (e.g., sulphapyrazine, sulphamerazine)	−	+	−

* But prevents completion of development in the mosquito.

The cinchona alkaloids, the 9-aminoacridines, and the 4-aminoquinolines have a destructive action on the asexual parasites of all forms of human malaria in the erythrocytic phase. The sulphonamides also act on this phase in *falciparum* infections, but in view of the risk of toxic effects, particularly of agranulocytosis, this class of drugs is not generally recommended for the routine treatment of malaria. Findlay (1949), however, recorded a complete absence of toxic reactions in a group of 441 British troops in West Africa who were given a daily dose of 50 mg. of sulphapyrazine, sulphamerazine, or sulphamezathine over a period of 12 months or more, the first-named giving results superior to those with mepacrine in the prophylaxis of malaria. He suggested that the sulphonamides might be found useful for this purpose should the local strains of parasite prove refractory to other drugs, or in a case of idiosyncrasy to other drugs.

The 8-aminoquinolines do not affect the asexual parasites in the erythrocytic phase, but exert a powerful destructive action on the gametocytes. They also act on the pre-erythrocytic phase, but only when employed in dosage dangerously high for routine use. The biguanides are the only known class of drugs which can be used with safety against this phase of the parasitic cycle. They also act on the asexual forms in the erythrocytic phase. They have no demonstrable effect on the gametocytes in the peripheral blood, but render them incapable of completing their development in the mosquito.

Prophylactic Treatment

The drugs used in the prophylaxis of malaria fall into two categories: (*a*) true causal prophylactics, which act on the parasite in its pre-erythrocytic phase; and (*b*) schizonticidal drugs, which destroy the asexual forms of the parasite in the erythrocytic phase and thus suppress the overt attack.

As stated above, the only drugs at present available which exert a true causal prophylactic action against malignant tertian malaria in non-toxic dosage are the biguanides, of which the best-known example is proguanil ("paludrine"). The dosage of proguanil recommended for prophylaxis is 100 mg. daily for non-immune individuals, and 300 mg. in a single dose once weekly for indigenous inhabitants of malarious countries. A great advantage of this drug is that

it can be placed in the hands of laymen for distribution without risk of ill effect, even should the prescribed dose be grossly exceeded.

The second, or suppressant, group of drugs includes the cinchona alkaloids, the 9-aminoacridines, and the 4-aminoquinolines. For the effective suppression of *falciparum* malaria quinine has to be administered in doses of as much as 10 gr. (0.65 g.) daily, which is the maximum that can be tolerated over a prolonged period. Against New Guinea strains of *P. falciparum* even this dosage has been found insufficient, failing to prevent overt attacks during the period of its administration. Apart from the unpleasant side-effects caused by the prolonged administration of quinine, the association of this drug with the precipitation of blackwater fever renders it undesirable for use as a suppressant in *falciparum* infections.

Mepacrine, in a dosage of 100 mg. daily, is a very effective suppressant of malignant tertian malaria, provided that the drug is taken for 14 days before exposure to infection and continued for one month after leaving the endemic area. It produces radical cure by schizonticidal action, destroying the young asexual parasites after their entry into the blood stream. The dramatic fall in malaria casualties during the later stages of the 1939–45 war in the South-West Pacific and in South-East Asia was chiefly due to the general adoption of mepacrine prophylaxis by the Allied Forces, and the rigid enforcement of this measure was an important factor in bringing about the successful conclusion of both these campaigns. It should be noted that neither proguanil nor chloroquine became available for general use until after the termination of hostilities.

Despite its powerful suppressant action, mepacrine has certain disadvantages which militate against its routine use under peacetime conditions. During the first 10 to 14 days of suppressive treatment a variable degree of nausea and abdominal discomfort is not uncommon. These symptoms usually disappear completely, but persist to some extent in a small proportion of cases. Headache, insomnia, and temporary giddiness may also occur during this stage, but are less frequent. When taking the drug over prolonged periods a proportion of individuals develop skin lesions, the most common of which is a lichenoid dermatitis affecting chiefly the hands and wrists and feet and ankles. Yellow discoloration of the skin is comparatively common; this is of no great moment among troops in time of war, but is a distinct disadvantage under peacetime conditions, particularly where women are concerned.

Chloroquine is a powerful suppressant, and excellent results have been reported with a dosage of 300 mg. of the base* administered in a single dose once weekly. Its action is similar to that of mepacrine, but it is said to be considerably less toxic and does not discolour the skin. The same advantages are claimed for camoquin, with a dosage of 500 mg. weekly.

At present the choice of drug for prophylactic use would seem to lie between proguanil and either chloroquine or camoquin. The stage in the parasitic life-cycle on which the drug exerts its action is of little interest to the individual under treatment, provided that the overt attack is prevented without any injurious side-effects, and from this point of view there is little to choose between the two classes of drugs. Chloroquine and camoquin, however, do not possess the very low grade of toxicity which is so remarkable a property of proguanil, rendering the last-named drug particularly suitable for widespread administration among labour forces or other employees recruited from indigenous populations.

*= 500 mg. of the diphosphate salt.

Treatment of the Clinical Attack

Most of the literature relating to the chemotherapy of malaria published during the last few years has been based on work initiated during the war period, when the overriding objective was the maintenance of the largest possible proportion of troops in a fit condition for the conduct of military operations. We have become accustomed to relate all our activities to their effect on the war effort, and it is not always appreciated that the objects of therapy in peacetime differ in certain important respects from those obtaining in time of war. Thus, in wartime minor toxic manifestations of drugs, or even an occasional case of severe toxicity, are of no great significance, since they do not affect the fighting efficiency of the troops to any appreciable extent. But in peacetime such occurrences are of very considerable importance, both to the patient and to the physician in charge of the case.

Again, in wartime a system of treatment which will control the clinical attack and effect radical cure in the great majority of malignant tertian infections may be considered adequate. But under peacetime conditions no treatment for this disease can be considered satisfactory unless it will ensure rapid alleviation of symptoms and a high rate of radical cure, not only in the "average" case but also in abnormally susceptible individuals exposed to heavy and repeated infection in hyperendemic areas. Finally, the provision of adequate treatment for indigenous populations, which is seldom practicable whilst military operations are in progress, is usually a major feature of antimalarial campaigns undertaken in times of peace.

Specific Treatment

The principal objects in the treatment of malignant tertian malaria are the termination of the clinical attack with the least possible delay, radical cure of the infection, minimum toxicity on the part of the drugs employed, and sterilization of gametocytes, so that mosquitoes which feed on patients during or after the attack cannot transmit the disease to other individuals.

Daily dosage of 20 to 30 gr. (1.3 to 2 g.) of quinine over a period of seven to ten days will usually bring about a rapid termination of the clinical attack and a high rate of radical cure. It is, however, comparatively ineffective against infections with certain European strains of *P. falciparum*. For example, James, Nicol, and Shute (1932) found that the amount of quinine necessary to control a primary attack of malignant tertian malaria caused by strains originating in the Roman Campagna and Sardinia was eight times as great as that required for infections with Indian strains of the same species of parasite. Quinine has no effect on the infectivity of gametocytes to mosquitoes, but a more serious disadvantage is that it may act as a contributory factor in the precipitation of blackwater fever. There was a striking reduction in the incidence of this disease among British troops stationed in West Africa after the substitution of mepacrine for quinine in the prophylaxis and treatment of *falciparum* infections (Findlay and Stevenson, 1944).

Mepacrine, when administered in the dosage now usually prescribed—i.e., beginning with a "loading" dose of 600 to 900 mg. on the first day or first two days of treatment, and continuing at 300 mg. daily for five to seven days—will effect a rapid termination of the clinical attack and a high radical cure rate in *falciparum* infections. The rapidity

with which this drug resolves the clinical symptoms of malaria has not in the past been fully appreciated, because until comparatively recently it has been the usual practice to prescribe a maximum of 100 mg. daily throughout the course, without a preliminary loading dose. Mepacrine does not, however, sterilize gametocytes; moreover, its toxic side-effects, though of rare occurrence, are by no means negligible. This applies particularly to the so-called mepacrine psychosis, which may be attended by symptoms of mental aberration or even of maniacal excitement (Findlay, 1947).

Chloroquine, like mepacrine, brings about rapid alleviation of clinical symptoms and a high rate of radical cure. It is said to be superior to both mepacrine and quinine in the treatment of *falciparum* infections, and to be relatively non-toxic in therapeutic dosage (Earle and Berliner, 1948). It has the advantage over mepacrine of not tinting the skin, and of being less likely to induce disagreeable gastro-intestinal symptoms. The regime recommended for adults is an initial dose of 600 mg. of the base, followed by an additional 300 mg. on each of the two following days. Camoquin, whose action resembles that of chloroquine, has been given in doses up to 400 mg. thrice daily for five days. Good results have also been reported with a single dose of 600–1,000 mg. Neither of these drugs renders gametocytes non-infective to mosquitoes.

Proguanil, in the absence of reinforcement with other drugs, has a less rapid action on the clinical attack than mepacrine, quinine, or chloroquine. Fairley *et al.* (1946a) recorded a high radical cure rate with New Guinea strains of *P. falciparum*, following a 10-days course of 300 mg. of proguanil daily; but against infections with a West African strain the drug failed to effect radical cure even when the daily dosage was raised to 600 mg. (Covell, Nicol, Shute, and Maryon, 1949). Reports from India, Malaya, Southern Europe, the Sudan, and Central Africa indicate that in these countries also there exist strains of *P. falciparum* which tend to recrudesce after a full therapeutic course of proguanil. The drug effectually sterilizes the gametocytes of *P. falciparum*, a property not possessed by mepacrine, chloroquine, camoquin, or the cinchona alkaloids. As already noted, it is by far the least toxic of all known antimalarial drugs.

As regards the choice of drug for treatment of the attack, none of those at present available fulfils all the requirements postulated above. Quinine has the disadvantage of its association with the precipitation of blackwater fever and is comparatively ineffective against certain geographical strains of *P. falciparum*. Mepacrine has a rapid and effective schizonticidal action, but is apt to produce a number of minor toxic manifestations and occasional psychoses of a more serious nature. Chloroquine and camoquin are probably the most powerful schizonticides, but occasional toxic manifestations have been recorded with each of them. None of these drugs renders gametocytes non-infective to mosquitoes.

Proguanil has a very low degree of toxicity and effectually sterilizes gametocytes, but, as we have seen, in the absence of reinforcement its action on the clinical attack is comparatively slow, and it cannot be relied upon to effect radical cure. It has, however, been demonstrated that when reinforced by mepacrine on the first day of treatment both these disadvantages can be overcome (Covell *et al.*, 1949). The dosage employed was 300 mg. of proguanil twice daily for 10 days, reinforced with 900 mg. of mepacrine given in three doses on the first day of treatment. It is possible that reinforcement by only 600 mg. of mepacrine would prove equally effective. It is considered unlikely that a single day's medication with this drug would be attended with any injurious side-effects, and it therefore seems probable that the above system of treatment would fulfil the main requirements for the treatment of malignant tertian malaria—namely, rapid alleviation of clinical symptoms, a high rate of radical cure, and sterilization of gametocytes, with minimal risk of injurious side-effects.

Reinforcement of the proguanil course with chloroquine or camoquin in place of mepacrine would probably prove at least as effective and might indeed prove superior. It is hoped that evidence on this point will shortly be forthcoming. Whatever form of treatment is adopted for the clinical attack, it is advisable to follow this up with a weekly maintenance dose of proguanil, chloroquine, or camoquin (100 mg. in each case) for six weeks to cover the period when recrudescences are most likely to occur.

For the dispensary treatment of indigenous populations in malarious countries, who possess some degree of tolerance to malarial infections, a single-dose treatment of 300 mg. of proguanil or chloroquine base or 600–1,000 mg. of camoquin has proved effective in a number of field trials. Chloroquine and camoquin are the more powerful schizonticides, but the exceedingly low toxicity of proguanil and its present comparatively low market price are powerful arguments in its favour. The extent to which each of these drugs is used will no doubt be determined very largely by the price at which they are eventually made available.

Allusion has already been made to the fact that different strains of *P. falciparum* may vary widely in their response to treatment with the same antimalarial drug. The Italian and Sardinian strains found by James, Nicol, and Shute (1932) to be resistant to quinine were readily susceptible to mepacrine. Similarly, Fairley *et al.* (1946b) encountered a strain of *P. falciparum* at Wewak, New Guinea, which proved resistant to mepacrine but highly susceptible to proguanil. The existence of strains which are naturally resistant or have acquired resistance to the action of proguanil has also been reported. It is therefore unwise to be dogmatic about the most suitable remedy for use against malignant tertian malaria in any particular circumstances, and it is fortunate that we now have at our disposal several specific antimalarial drugs, so that should a strain of parasite resistant to one of them be encountered it may be replaced or reinforced by one of the others.

General and Emergent Treatment

Whatever specific treatment is prescribed, the patient should be confined to bed during the attack and the bowels kept open by small doses of calomel, followed by salts in the morning if found necessary. The diet should be restricted to fluids during the height of the fever, glucose being given freely if available. In the event of a rigor, hot-water bottles and several blankets are indicated. Hyperpyrexia may necessitate cold sponging. The headache may be relieved by aspirin, caffeine, codeine compound, or phenobarbitone.

Pernicious forms of malignant tertian malaria, whether cerebral, algid, or gastro-intestinal, require special treatment. In such cases the oral administration of drugs is seldom practicable, and, since prompt action is necessary to save the patient's life, they must be given parenterally. Quinine dihydrobromide or dihydrochloride, 10 gr. (0.65 g.) in 20 ml. of normal saline, may be injected intravenously *very slowly*, not more than 2 ml. per minute by the watch.

repeated in six to eight hours if necessary. Mepacrine sulphonate (atebrin musonate) may also be given intravenously, but the margin of safety with this drug is low, and the intramuscular route is to be preferred, 200 mg. being injected into each buttock (total dosage 400 mg.). Good results have also been claimed with chloroquine and camoquin given intramuscularly. Should none of the above-mentioned drugs be available, quinine sulphate 15 to 30 gr. (1 to 2 g.) may be given per rectum, mixed with starch paste thin enough to run through a rectal catheter. The drug is rapidly absorbed by this route. As soon as the patient is able to take drugs by mouth all further medication should be administered orally. The action of proguanil is not sufficiently rapid to warrant the use of this drug in cases of extreme urgency.

Blood transfusion may be indicated in pernicious malaria accompanied by grave anaemia. Vomiting, if persistent, may be relieved by intravenous injections of 5% glucose in 200 to 400 ml. of normal saline, repeated if necessary, and supplemented by 1 mg. of thiamin hydrochloride for each 25 g. of glucose.

Summary

The relative merits of the various specific drugs now available for the treatment of malignant tertian malaria are discussed in detail.

Emphasis is laid on the importance of differentiating this disease from a number of others which it may simulate very closely, and on the fact that infections with different geographical strains of *P. falciparum* may vary widely in their response to treatment with the same antimalarial drug.

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The control of venereal diseases in Germany was one of the most arduous tasks which faced the Occupation Authorities after the war. In an article which appeared in a recent number of the *Epidemiological and Vital Statistics Report*, Dr. T. Guthe, Chief of the Venereal-Disease Section of WHO, surveyed the situation in Germany from 1945 to 1948, and gave a detailed account of the result of measures taken in the various zones during that period. According to the *Chronicle of the World Health Organization* the venereal-disease problem in Germany is not due to the presence of occupying troops and displaced persons, although this view is often expressed by Germans. Venereal diseases increased steadily in Germany, as in other countries, as a consequence of war conditions : displacement of civilian, industrial, and military populations; social, economic, and political upheavals; disruption of family life; increase of promiscuity and prostitution. Surveys carried out at Frankfurt-on-Main and Hamburg show that venereal diseases caused considerable ravages among the civilian population during the war. The increase in venereal infections which took place during the war in civilian and military populations in the Reich was also observed in several countries occupied by or allied with Germany, as recorded in Denmark, Finland, France, Greece, Norway, and some of the Balkan countries.

CONTINUOUS CAUDAL ANALGESIA IN OBSTETRICS, SURGERY, AND THERAPEUTICS*

BY

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The extradural administration of local analgesic solutions through the sacral hiatus via an indwelling malleable needle or an indwelling small-bore catheter is designated as continuous caudal analgesia. The basic technique of single-injection caudal analgesia produced by a cocaine solution was independently introduced in Paris in 1901 by J. A. Sicard and F. Cathelin. As new and safer local analgesic agents were developed, modifications of the technique greatly extended the anatomical application of this method to nerves of pain in, first, the sacral plexus, then the lumbar region, and, finally, to the low and mid-thoracic regions. Even though caudal analgesia provided a high percentage of successes in rectal surgery and in urology, it was so undependable in obstetrics that Stoeckel abandoned it shortly after he introduced it in 1909. Dr. Hans Schlimpert, of the Freiburg Clinic, developed a satisfactory technique of caudal analgesia in obstetrics, which was used in combination with *Dämmerschlaf*. His tour of American clinics in 1913 stimulated the application of this method in a few centres.

In America during the next three decades the single-injection technique of caudal analgesia was enthusiastically utilized but ultimately rejected by all except one of its outstanding advocates. The one exception was my own revered professor of anaesthetics, Dr. John S. Lundy, of the Mayo Clinic. It was Lundy who instructed me in my first applications of this technique. It was he who inspired me with the thought that all pain can be conquered if the physician will master the science of applying the principles of pharmacology and anaesthesiology to the specific anatomical pathways of pain.

Thus in 1940 and 1941, when uncontrolled obstetric pain on the one hand, and profound and prolonged obstetric narcosis on the other, demanded a more satisfactory and safer method of anaesthesia for the parturient woman and her baby, Southworth, Edwards, and I surveyed the problem to determine the specific nerve pathways involved. We found that the classic researches of John G. P. Cleland, of McGill, had delineated the afferent pain pathways of the contracting uterus as passing through the eleventh and twelfth thoracic nerves. We substantiated the postulates of Sir Henry Head, of England, that pain of the dilating cervix was transmitted through the second, third, and fourth sacral nerves. We concurred with DeLee, Greenhill, and Tucker that the pain of perineal distension was transmitted through the pudendal, perineal, and haemorrhoidal nerves. We soon found that the single-injection technique of Sicard and Cathelin when extended to the tenth thoracic segment in the peridural space would totally relieve temporarily the pain of labour or the pain of delivery.

Merely by combining the principles of caudal analgesia with the continuous spinal anaesthesia principle of Lemmon, of Philadelphia, and the continuous aortic lumbar anaesthesia of Abruel, of Rumania, we were able to fashion a

*Read in opening a discussion in the Section of Anaesthetics at the Annual Meeting of the British Medical Association, Harrogate, 1949.

new technique: continuous caudal analgesia. Thus, for the first time it was possible to control the pain of the major portion of active labour and that of delivery with the same technique. Happily, such a technique at the same time removed from the baby the burden of transplacental narcosis. It has been described in the following manner by Dr. J. P. Greenhill in his last edition of DeLee's *Obstetrics*: "There is no doubt that when this procedure is properly performed without any misstep there is no more satisfactory and pleasant type of analgesia in obstetrics."

It is obvious, therefore, that continuous caudal analgesia represents the combined efforts and brilliant researches of two distinguished French physicians, a Canadian obstetrician and anatomist, an English neurologist, German, Swiss, and American pharmacologists, a Mayo Clinic anaesthesiologist, a Philadelphia surgeon, and a Rumanian physician, who have placed in our hands the principles, the drugs, and the anatomical knowledge necessary to develop a single technique that is capable of relieving pain for surgery, obstetrics, and therapeutics from the xiphoid to the toes for an hour, a day, or a week.

Among the architects of this technique it would be impossible to overlook the substantial contributions of that venerable metallurgist and artisan, Oscar Schwidetzky, of the Becton Dickinson Company, who has fashioned with ingenuity the simple and compact instrumentarium.

Use in Obstetrics

The outstanding advantage of continuous caudal analgesia in this field is seen in a baby delivered without trauma, who cries and breathes and saturates his blood cells with oxygen without stimulation. This factor of baby protection is unequalled in any form of seminarcosis, narcosis, or general anaesthesia. It can be approximated only by saddle-block spinal anaesthesia and local analgesia. After a personal experience with this technique in 12,000 cases, and after training 2,000 physicians, who have reported its use in 260 scientific papers in eight languages for 600,000 deliveries, I am convinced that it offers effective and humane relief, without suggestion or hypnotism, to normal and handicapped mothers for the delivery of normal and premature babies. This opinion is shared by the 80 American obstetricians who have each managed more than a thousand deliveries under continuous caudal analgesia.

The leading United States hospitals which utilize this technique in substantial numbers are: the Beth-El Hospital in Brooklyn with 12,000 cases; the Stanford University Hospital in San Francisco with 8,000 cases; the Philadelphia Lying-in Hospital with 5,000 cases; the Syracuse University Hospital with 10,000 cases; the United States Marine Hospital in New York with 2,000 cases; the Johns Hopkins Hospital with 2,000 cases; the hospitals of Memphis, Tennessee, with 5,000 cases; the Barnes Hospital in St. Louis with 3,000 cases; and many others where nurses or doctors, trained on a 24-hour team basis, utilize this technique correctly, with the medical safeguards which protect the altered body processes in a psychological environment which maintains the patient's happiness and emotional tranquillity.

The new adjuncts of this order provided for our patients, who so often are mentally alert and who are enthralled in observing with a clear eye the actual birth of their babies, are: air-conditioning, bedside libraries, interior decorating in pastel colours, landscapes in oils and water colours, television, and well-controlled and well-selected melody and symphony of transcribed music. All or none of these pleasant interludes are provided at the direction and prescription of the attending obstetrician and of the patient herself.

Continuous caudal analgesia has returned to womankind the privilege of being present in comfort for the baby's birth. Its judicious use provides the safest labour and delivery available for patients with cardiac disease, nephritis, pulmonary disease, metabolic disease, and toxaemia. More than a score of outstanding obstetricians have declared continuous caudal analgesia to be the physician's best invitation to a premature baby for survival. In documenting this statement the Washington University Maternity Hospital from St. Louis, in a study of 591 premature deliveries (Table I), reported recently to the American Medical Association that "the labours protected by conduction anaesthesia (three-quarters under caudal and one-quarter under saddle-block) show an infant mortality that was consistently at least 100% lower than that in the non-conduction group."

TABLE I.—*Results of 591 Premature Deliveries Among 7,650 Non-conductions, 2,500 Caudal, and 500 Saddle-block Deliveries (July 10, 1945, to December 27, 1948)*

Weight Group	Total No. in Group	Intranatal Deaths	Post-natal Deaths	Neonatal Deaths	Total Deaths	Infant Mortality
Non-conduction Group						
2,500–2,001 g.	218	5	3	9	17	7·8%
2,000–1,501 g.	75	5	1	11	17	22·7%
1,500–1,001 g.	34	6	1	11	18	52·9%
1,000–500 g.	20	10	5	5	20	100·0%
	347	26	10	36	72	20·8%
Conduction Group						
2,500–2,001 g.	138	1	0	4	5	3·6%
2,000–1,501 g.	65	0	1	3	4	6·2%
1,500–1,001 g.	28	0	0	7	7	25·0%
1,000–500 g.	13	1	0	9	10	76·9%
	244	2	1	23	26	10·7%

Incidence of premature deliveries in the non-conduction group is 4·9% (35 stillborn macerated infants included), and in the conduction group 8% (5 stillborn macerated infants included).

My experience during a three-year study, 1942–5, in the Philadelphia Lying-in Hospital coincided substantially with the Washington University report (Table II). It is my belief that if delicate premature infants, who comprise approximately 10% of obstetrical deliveries, are protected by this technique the mature babies might receive the same relative benefit.

TABLE II.—*Neonatal Mortality per 1,000 Live Births Among Full-term and Premature Infants in the Caudal and Control Groups*

	Premature Infants	Full-term Infants
Control group	227·3	6·4
Caudal group	131·7	3·0

The Philadelphia and Memphis studies show that mothers in all age groups, but particularly in the early and late extremes of the child-bearing period, benefit from this form of management (Tables III and IV).

Use in Breech Delivery.—One of my first students, Dr. Roy Nicodemus, director of obstetrics of a large Pennsylvania hospital, six years ago began the routine use of continuous caudal analgesia. In 4,000 consecutive deliveries with this technique he has managed 186 breech deliveries with an uncorrected infant mortality of stillbirths and neonatal deaths of 1.2%. He then analysed the previous 186 breech deliveries in which he had used general anaesthesia and sedation and found an uncorrected infant mortality of 6.9%. In a paper soon to be published in the American literature he concludes that this method thus lends itself favourably to the safe management of breech delivery.

Table III.—*Stillbirths and Neonatal Mortality per 1,000 Live Births Among Mothers of Different Ages in the Caudal and Control Groups. Philadelphia Study*

	Age of Mother		
	Under 25	25–29	30 and Over
Control group	47·8	30·6	59·0
Caudal group	14·2	13·6	35·4

Table IV.—*Stillbirths and Neonatal Mortality (Under 1 Week) per 1,000 Live Births Among Negro and White Mothers of Different Ages. Memphis Study, 1946*

	Age of Mother		
	Under 25	25–29	30 and Over
General	45·1	159·1	131·1
Spinal	70·8	46·5	60·0
Caudal	32·0	40·0	52·6

Use in Therapeutics

Continuous caudal analgesia through its control of nerve impulses to blood vessels and extremities and to viscera of pelvis and abdomen can be utilized as a major therapeutic measure. Its most promising field of usefulness lies in the following diseases: (1) the control and treatment of eclampsia, (2) oliguria and anuria on the basis of reflex renal ischaemia, (3) post-surgical abdominal distension and paralytic ileus, (4) arterial emboli of abdomen and lower extremities, (5) thrombophlebitis and phlebothrombosis, (6) prognosis of and indications for sympathectomy in essential hypertension, (7) the prolonged relief of post-operative or traumatic pain, and (8) sciatica and neuralgias of the lower extremities and pelvic girdle.

In 24 consecutive cases of eclampsia managed by me in the John Gaston Hospital in Memphis, Tennessee, there was a reduction in both the systolic and the diastolic blood pressures, and there was definite clinical improvement and elimination of convulsions in each case so treated. These 24 cases form part of a series of 76 that I have managed with these techniques in which there were only three maternal deaths. The infant mortality in this series was 12%. It is my contention that the substitution of continuous conduction anaesthesia for narcotic and magnesium sulphate therapy in eclampsia provides the most effective method of blood pressure and convulsion control, and permits the highest incidence of live births in this group.

A related type of vasomotor crisis is seen in the terminal coma with convulsion associated with uraemia and glomerulonephritis. An 11-year-old negro girl had a persistently mounting blood pressure, with ultimate heart failure and pulmonary oedema in spite of sedation with "aminophylline" and intravenous magnesium sulphate therapy, and even phlebotomy of 200 ml. At the point of *exodus letalis* continuous caudal analgesia in fifteen minutes, according to the indicated dosage schedule, reduced the blood pressure from 215/185 to 140/90, with the prompt restoration of consciousness, improvement of urinary outflow, and control of the pulmonary and cardiac emergencies.

Continuous caudal analgesia has presented us with an avenue of therapeutic inhibition of critical neurogenic and angiospastic mechanisms. Upon this concept lies a new horizon for the medical profession which may supersede the use of this technique in the control of pain. Its companion is the anatomically related continuous lumbar peridural analgesia as designed by us.

As continuous caudal analgesia exerts its most profound influence from below upward over the spinal nerves, so does lumbar peridural analgesia exert its influence from above downward. Either of the techniques presents the exact anatomical avenue for anaesthesia or for therapy of the organ or segment involved.

Use in Surgery

Continuous caudal analgesia is the safest and most effective technique at our disposal for operative and post-operative pain relief in haemorrhoidectomy, prostatectomy, and for operations on the perineum. By extending the levels of nerve block into the low thoracic plexus, adequate anaesthesia is produced for hernioplasty, appendicectomy, and caesarean section. We have utilized this technique in the latter three operations in more than 2,000 patients without any anaesthetic mortality. Now with continuous peridural lumbar analgesia at our disposal upper-abdominal and low-thoracic operations are more widely being managed by the extradural approach. In our hands this technique has been particularly useful for the control of pain in long orthopaedic operations which require serial *x*-ray confirmations of position and alignment of dismembered bony fragments. Even the aged and debilitated patients withstand hip-nailing operations and the like with the minimum of shock under this technique.

Drugs and Techniques.—Both techniques of the malleable needle and the indwelling catheter have been thoroughly described in the literature. The most practical recent improvement has been the substitution of the economical plastic catheter. We have extended dosage schedules and optimum concentrations of procaine, "metycaine," "pontocaine," "nupercaine," and, more recently, the safe and effective local analgesic from Sweden that is being introduced as "xylocaine."

Purely on an anatomical basis we can effectively block the afferent nerve pathways from the respective organs with the indicated dosage:

Haemorrhoids and rectum	10 ml.
Prostate and perineum	20 ml.
Bladder and uterus	30 ml.
Appendix and intestine	40 ml.
Stomach, spleen, and gall-bladder	50 ml.

Continuous caudal analgesia can be intensified to a nerve block comparable with that obtained with spinal anaesthesia by a second dose, according to the scale indicated, about fifteen minutes after the first. The duration of the analgesia is entirely dependent upon the number of serial doses that are used.

Complications, Dangers, and Contraindications

Of utmost importance is a thorough knowledge of prevention of complications, amelioration of the hazards, and strict observance of the contraindications.

The most common complication is the slow or arrested labour that develops from two factors: (*a*) too early institution of the technique before progressive dilatation of the cervix to 5 cm.; and (*b*) overdosage extending the level of analgesia into mid-thoracic and upper-thoracic levels, thus interfering with the motor innervation of the uterus.

Fortunately, with the continuous method instituted through the indwelling small-gauge catheter the analgesia may be permitted to wear off and then be withheld until there is evidence of established and progressive labour. The analgesia should not be persistently maintained in the event of retarded labour unless a therapeutic advantage to either mother or baby is seen.

In my clinical experience, which is substantiated by both the Lorand and Reynolds tocodynamometer studies, approximately one-third of the labours are retarded to a

varying degree with standard dosage and segmental block; one-third are unaffected; and one-third actually suggest a clinical improvement in progress and dilatation. The second stage is definitely prolonged, since the compulsion desire to push and the abdominal somatic tone are both diminished. The usual primipara with the normal-size infant in the United States is delivered by election with episiotomy and outlet forceps. Most multiparae may be encouraged to deliver spontaneously.

The second highest complication incidence is the development of maternal hypotension, especially in the dorsal supine position. In large measure this is mechanical, through the production of a bloodless phlebotomy into the dilated vessels of the lower extremity. In some 5,000 carefully analysed cases this complication presented itself in 22% of the cases. The usual range of systolic reduction was from 120 to 90 mm. Hg.

The incidence may be greatly decreased by the prophylactic use of the vasopressor drug in all individuals with normal or low blood pressure, and in the maintenance of proper hydration, especially during hot weather. Hypotension may be combated by: (*a*) intravenous vasopressor drugs in minute 10-mg. doses of ephedrine or the equivalent *pro re nata*, (*b*) intravenous fluids containing glucose, (*c*) high atmospheres of inhaled oxygen, and (*d*) autotransfusions by raising the lower extremities to right-angles with the long body axis to produce a gravity return of the venous blood. In cases with severe varicose veins elastic stockings should be applied.

In our experience the mother tolerated extremes of hypotension, even a systolic pressure of 60 mm. Hg, better than the baby, who on occasion developed a bradycardia when a maternal systolic pressure below 80 mm. Hg was neglected for five minutes or longer. Even under these circumstances we have delivered babies with normal arterial and venous cord blood oxygen, provided the mother at the time was inhaling rich oxygen atmospheres. A few cases of loss of foetal life *in utero* or shortly thereafter have emphasized to several observers the importance of maintaining maternal blood pressure.

A third complication formerly greatly feared is the inadvertent spinal or subarachnoid anaesthesia of overwhelming proportions with the usual caudal dosages. The institution of the test dose and the ten-minute wait before proceeding and the institution of a low, safe, continuous spinal or saddle-block analgesia for these cases through intentional election have served to minimize this hazard. Inadvertent puncture of the spinal canal, with the usual insertion of a needle 6 cm. into the canal, has occurred under supervision only about once for each 500 cases. In some we elect to abandon the procedure, but in others we prefer to institute continuous spinal analgesia with usually one-thirtieth to one-fifteenth of the recommended dose. Careful aspiration of the indwelling caudal needle before insertion of the catheter reveals spinal fluid in almost all the small fraction of cases with low-lying durae.

Another complication that was formerly greatly feared is infection about the site of injection. With careful cleanliness and antisepsis and gloved technique, the incidence of infection is now about 1 in 1,000 caudal deliveries. The majority of these are simple pin-point pustules from the needle puncture. About one case of cellulitis or peridural infection occurs in each 5,000 deliveries under continuous caudal analgesia. With the prompt institution of the antibiotic drugs this type of infection can often be controlled. Nevertheless, with proper technique and proper care of equipment it can be prevented. In the control of eclampsia we have maintained continuous caudal analgesia for periods of one week without producing any demonstrable nerve irritation.

The fifth type of complication is that due to individual toxicity to the various local analgesics. It is characterized by immediate and persistent nausea and vomiting accentuated by each dose of the local analgesic, by tachycardia, by dizziness, and by hyperirritability. In nearly every instance we have achieved satisfactory results by the substitution of another local analgesic, such as procaine or pontocaine for metycaine, or vice versa.

The contraindications are as follows: (1) inadequate training or skill on the part of the operator; (2) substandard home or hospital conditions which do not provide the safeguards of available oxygen, vasopressor drugs, intravenous fluids, and proper asepsis; (3) local infection or skin irritation at the site of needle puncture; (4) gross abnormalities obliterating sacral hiatus or deformities of the vertebral column, which preclude the proper distribution of the anaesthetic agent; (5) central nervous system disease or disease of the vertebral column, such as tuberculosis, syphilis, etc.; and (6) previous laminectomy.

Summary

In America continuous caudal analgesia has been used for more than 600,000 deliveries. It has proved its capacity for relieving pain in surgery, obstetrics, and therapeutics from the xiphoid to the toes for an hour, a day, or a week. Its proper application eliminates transplacental narcosis and pharmacological retardation of vital baby reflexes.

Through such a mechanism of labour the premature baby is spared drug depression and the traumas attendant upon delivery through an unrelaxed birth canal.

More than 200 medical papers in eight languages have concluded that infant mortality and morbidity have been reduced with continuous caudal analgesia.

Under its management the third stage of labour is shortened and post-partum blood loss approaches the minimum. Post-partum complications are conspicuous by their absence.

Mothers with toxaemia, heart disease, and respiratory and metabolic infirmities are spared most of the stress and strain of labour.

It has been used in the control and treatment of eclampsia in more than 100 cases, with a maternal mortality below 5% and an infant mortality below 15%. Dieckmann, of Chicago, has described it as the outstanding advance in the treatment of this disease of our present decade. Greenhill, of Chicago, has declared: "There is no more satisfactory and pleasant type of analgesia in obstetrics."

The indwelling-catheter method of administration makes it simple and easy to apply for prolonged periods.

In proper dilutions all of the standard local analgesic agents in volume sufficient to block the 16 afferent nerve pain pathways from the uterus provide complete maternal comfort in 85 to 92% of cases.

The complications have been sharply delineated and methods of their prevention and treatment are presented.

The incidence of forceps deliveries is increased. In those clinics where this is considered to be undesirable this technique will still prove to be invaluable in permitting slow deliberate forceps delivery of the parturient woman arrested in the second stage of labour.

The technique has been used successfully for all types of rectal, perineal, and lower abdominal operations and for orthopaedic procedures on the lower extremities.

In the treatment of thrombophlebitis it provides easy access to the sympathetic nerves, which Leriche blocked through the paravertebral approaches. In America continuous caudal analgesia with a single-needle catheter technique is replacing the four needle insertions of lumbar paravertebral block.

Other therapeutic applications in treating arterial emboli, reflex anuria, abdominal distension, and vascular insufficiency have been described.

Continuous caudal analgesia has been determined of great value in the prognosis of sympathectomy for essential hypertension.

It opens a new avenue for the prolonged control of post-operative and intractable pain in terminal carcinomatosis.

Finally, the medical profession and I personally express our gratitude to our European colleagues who in 1901, after careful researches, made possible this medical technique which it has been my privilege to extend into these various applications.

SOME OBSERVATIONS ON PULMONARY TUBERCULOSIS IN THE NIGERIAN AFRICAN

BY

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Pulmonary tuberculosis is moderately common amongst the Nigerians, but, though cases now report more often to the hospitals for treatment, there is no conclusive evidence that its incidence is rising significantly. Anticipated measures for the control of the disease in Nigeria are likely to meet with little success unless close account is taken of its particular characteristics in the African, and it is hoped that the following observations may serve to stress some of its features. The series of cases, though consecutive, is admittedly very small, but supports the conclusions drawn from a large number of additional cases seen during the last eleven years, but in which observations and investigations were less complete.

The peculiarly virulent nature of pulmonary tuberculosis in the African is still sometimes attributed to a relatively recent introduction of the infection by the European to a country and people not hitherto exposed to it—a so-called virgin soil. It is probable, however, that the disease was introduced long before the advent of Europeans in significant numbers, possibly from the North and Near East by the old trans-Sahara trade routes. Conceptions of the importance of a virgin soil seem to imply that an inherited immunity can be established as a result of several generations of exposure to infection, but the example of the American negro furnishes no evidence in support of this supposition or in favour of a possible progressive genetic elimination of the highly susceptible. Though improvement in education, economic status, and standard of living may do much to mitigate the severity of the disease amongst the population as a whole, it seems that the violence of the disease in the African must be explained on a basis of his inborn constitutional peculiarities.

The common impression in Nigeria is that pulmonary tuberculosis in the African is not amenable to treatment and is invariably fatal. That the outlook is not so hopeless as this Davies (1946) has shown as a result of twenty years' work in Tanganyika. He points out that by the time a patient presents himself voluntarily for treatment his disease, so rapid is its advance in the African, is already hopeless of cure, and such indeed is the experience in Nigeria. Apart from the obvious necessity for education of the public and for improved living conditions, isolation of the open case is a prime essential. Davies stresses that for this purpose, and for the detection of cases early enough for effective treatment, sanatoria working as isolated units are no more effective than the existing general hospitals, for both are dependent on the voluntary attendance of patients. Only by the institution of travelling teams equipped for clinical examination, mass skin tests, and miniature radiography, designed to detect the early case and the susceptible individual, and of spaced bush dispensaries based on regional sanatoria, can satisfactory results be anticipated.

Incidence of Tuberculous Infection

Skin Tests.—Table I shows the results of Mantoux tests with 1 in 5,000 old tuberculin on 93 hospital in-patients, chiefly Northern Nigerians, not exhibiting any demonstrable tuberculous lesion. Table II gives the Mantoux results with 1 in 500 old tuberculin in 43 similar in-patients, while Table III shows the findings with 1 in 500 old tuberculin in 93 male scholars of a Government secondary school, all Southern Nigerians aged between 13 and 16 years. It is evident from these results that 65% of the more urban sections of the community in their mid-teens and 80% of those in the 20–29 age group and onwards have experienced a tuberculous infection.

TABLE I

Age Group	0–9	10–19	20–29	30–39	40–49	50 and Over
Positive	0	6	13	7	13	8
Negative	3	13	9	7	9	5
Proportion positive ..	0%	32%	59%	50%	59%	61%

TABLE II

Age Group	0–4	5–9	10–14	15–19	20–29	30–39	40–49	50 and over
Positive	1	2	2	3	8	3	4	4
Negative	4	5	1	1	2	1	1	1
Proportion positive	20%	29%	67%	75%	80%	75%	80%	80%

TABLE III

Negative	Weakly Positive	Strongly Positive	Total Positive
32	10	51	61 (65·6%)

Necropsy Evidence.—In a series of 90 consecutive routine necropsies carried out on the cadavers of patients who had died in one hospital of conditions other than tuberculous a search was made for latent or healed tuberculous foci. Almost all of the lesions so encountered were sent to the Lagos laboratory for microscopical confirmation. The results are given in Table IV.

TABLE IV

Age Group:	0–9	10–19	20–29	30–39	40–49	50 and over	Total
Pulmonary focus ..	0	0	0	1	1	1	19 (21·1%)
Hilar or broncho-mediastinal gland focus	0	0	3	1	2	1	
Pulmonary + hilar gland foci ..	0	0	0	1	1	1	
Abdominal gland focus	0	0	2	1	1	0	
Pulmonary, hilar gland, and abdominal gland foci ..	0	0	1	1	0	0	
No tuberculous focus	6	6	18	13	20	8	71 (78·9%)
Proportion with tuberculous foci ..	0%	0%	25%	28%	20%	27%	

It is observed that of these 90 cadavers 19 (21.1%) showed easily demonstrable healed or latent tuberculous foci. The employment of specialized methods would

undoubtedly have revealed a far higher percentage. The pulmonary lesions were usually subpleural and most commonly took the form of small gritty areas of fibrosis and anthracosis containing caseous foci from the size of a pinhead to ¼ in. (0.3 cm.) diameter. Larger encapsulated caseous foci were much less common. In the case of the hilar gland lesions the glands were usually a little enlarged, anthracotic, and contained similar pinhead, grey or yellow caseous foci. The abdominal glandular lesions are of some interest, as milk rarely enters into the dietary of these people, and in one or two cases the site of the lesions was not altogether suggestive of an intestinal portal of entry. Thus one cadaver with tiny caseous foci in the left upper lobe and associated broncho-mediastinal glands exhibited also gross enlargement and old caseation in glands at the root of the mesentery. A second showed tiny caseous foci in two of the right para-aortic abdominal glands as the only demonstrable tuberculous focus. Old pleural adhesions were encountered in 75% of the cadavers.

Clinical and Necropsy Observations in Cases of Pulmonary Tuberculosis

The clinical and post-mortem findings in 36 consecutive cases of tuberculosis with pulmonary lesions treated in one hospital have been analysed and summarized. Patients admitted during this period who absconded or on whom necropsy was refused have been excluded. The patients were Northern and Southern Nigerians, with a considerable preponderance of the former. Although the disease pursued an essentially similar course in the two races, it was the impression that the Northerners showed a rather lower resistance than the Southerners. Complicating factors are always common in these people, malaria being universal, intestinal helminths almost invariable, and filariasis, bilharziasis, dracontiasis, chronic amoebiasis, and malnutrition occasional. By clinical and necropsy criteria five types of case could be distinguished, the respective features of which are detailed below.

Type 1

This group comprised 23 cases, the extremes of age being 18 and 64, and the average age 36. Seven patients were over 45. All complained of productive cough, weakness, and weight loss, several of diarrhoea, six of hoarseness due to associated laryngitis, six of chest pain, and only three of haemoptysis. In all there were obvious physical signs in the chest, usually bilateral, and in all the sputum was profuse and acid-fast bacilli were easily found, often in large numbers. All cases showed a moderate to severe hypochromic anaemia, and in over half the cases there was a leucocytosis of 12,000 to 16,000, usually with a polymorphonuclear percentage of between 75 and 90, and no monocytosis. It should be mentioned that in 44 average healthy Africans the mean white cell count was found to be 6,807 (polymorphonuclear neutrophils 59%, lymphocytes 31%, monocytes 4.6%, eosinophils 4.4%).

In all cases in which it was determined the B.S.R. was between 50 and 70 mm. in one hour, except for one of 20 mm. and one of 2 mm. All showed some pyrexia, remittent or intermittent, with evening rises to 100–102° F. (37.8–38.9° C.). Weight loss varied between ½ and 3 lb. (0.22 and 1.36 kg.) per week, and the average interval between the alleged onset of symptoms and death was seven months, the extremes being two and 13 months. Admittedly this estimate of the average duration of life excludes a few of the less severe cases, in which the patients, either because of lack of progress in hospital or because treatment had resulted in sufficient amelioration to induce in them undue optimism, absconded and were excluded from the series.

I have, apart from the present series, kept more favourable cases under observation and treatment for as long as two years before they defaulted in their attendance. Yet I have never, under existing conditions, encountered a case that had been permanently cured or offered promise of being so. As regards treatment, I have during the last ten years employed collapse therapy, artificial pneumothorax, often bilateral and partial, alone or in combination with phrenic evulsion, in a considerable number of cases. The majority of the patients showed bilateral involvement, were too advanced to be truly suitable, and derived no significant benefit. However, the few less hopeless cases showed enough improvement to suggest the probable effectiveness of collapse therapy if cases could be detected and brought under treatment at an earlier stage. Suitable antibiotics have not been available.

At necropsy there was very extensive cavitation of one or both upper lobes. Often the whole of one upper lobe would be represented by a huge cavity bounded only by the greatly thickened and densely adherent pleura. Evidence of fibrosis limiting the cavities before the pleura was reached was very rare and never marked, except in one case which showed sufficient gross fibrosis to produce tracheal displacement. Exceptionally, cavitation was more extensive in a lower lobe. The condition of the remaining lobes was variable, but rarely were they normal and healthy. Very often there were more or less large areas of whitish caseous pneumonic infiltration, sometimes, when extensive, with central cavitation. Often there were isolated clean-cut spheroidal cavities about 1 in. (2.5 cm.) in diameter and containing fluid pus.

In most cases there were the scattered diffuse single and trefoil lesions of tuberculous bronchopneumonia. Occasionally a lobe might have an appearance of hepatization. The hilar glands were fibrotic and anthracotic, but rarely showed macroscopic tuberculous lesions. There were in the majority typical tuberculous ulcers of the ileum, with white thread-like infiltration of the associated lymphatics and caseous foci in the regional mesenteric glands. Apart from this latter, gross lympho-glandular lesions were absent, as also were miliary lesions. In only three instances were primary tuberculous foci detected. One showed a typical Ghon lesion at the left apex, and in the right upper lobe several old inspissated caseous foci, some partly calcified, varying in size from a pinhead to a peanut and surrounded by considerable fibrosis. Another showed old pinhead foci of caseation with surrounding fibrosis and anthracosis in an upper lobe, and the third two mesenteric glands converted to mere fibrous shells enclosing old inspissated caseous matter.

Type 2

Eight cases fell into this group; the ages ranged from 17 to 42, the average being 29. The invariable complaints were of productive cough, weakness, and weight loss. Obvious clinical chest signs were present in all, and acid-fast bacilli were always found in the sputum, usually in profusion. The blood count as a rule was characterized by a moderately severe hypochromic anaemia, and in five cases a leucocytosis of from 11,700 to 25,600 with polymorphonuclear percentages from 74 to 91 and no monocytosis. The B.S.R. lay between 60 and 70 mm. in one hour in all cases except one, in which it was only 3 mm. Pyrexia was remittent or intermittent, with rises to 101–103° F. (38.3–39.4° C.); the average weekly weight loss was 2½ lb. (1.13 kg.); and the average interval between the professed onset of symptoms and death 4½ months, the extremes being 1½ and eight months.

The common necropsy finding was very extensive areas of whitish tuberculous caseous pneumonia with small or moderate-sized central cavities where the caseous matter had broken down. The intervening lung might have an appearance of grey or gelatinous hepatization, while often the tiny diffuse lesions of tuberculous bronchopneumonia were found elsewhere. Tuberculous ileal ulcers with caseation of the associated mesenteric glands were usually present. There was always gross enlargement and caseation of broncho-mediastinal and/or cervical and abdominal lymphatic glands. Seven of the cases showed miliary lesions in one or more of the liver, spleen, and kidneys, and while the hepatic and renal lesions were typical milia the splenic foci were often larger, up to about ¼ in. (0.6 cm.) in diameter. Three cases showed primary tuberculous foci —one a caseous pulmonary area ½ in. (1.25 cm.) in diameter with surrounding fibrosis and anthracosis, and the other two

small yellow caseous pulmonary foci from the size of a pinhead to ¼ in. diameter with surrounding fibrosis.

Type 3

There was only one case of this type, that of a man aged 34 who had complained of retrosternal pain and unproductive cough for two weeks. He was found to have a pericardial effusion and congestive cardiac failure, and died within a few days. At necropsy a grossly thickened parietal pericardium was found and an equally thickened and shaggy visceral pericardium, reported microscopically as tuberculous. The right lower lobe pleura was adherent and the upper lobe pleura opaque and markedly thickened. In the hilar zone of the right upper lobe were cavities the size of a peanut filled with old caseous matter; more peripherally were a few pinhead caseous foci and dense fibrosis of the whole area. This was reported by the pathologist as "a very chronic tuberculosis with great fibrosis and hyaline degeneration." In the right lower lobe and both left lobes were a few scattered pinhead caseous foci; in the left upper lobe there was an encapsulated caseous focus the size of a peanut. The hilar and broncho-mediastinal glands were a little enlarged and anthracotic, and contained small caseous foci. The mesenteric glands were enlarged and yellowish, and showed caseous areas.

Type 4

There were three patients in this group, aged 17, 19, and 27. The complaint in all cases was of weakness, weight loss, and cervical swellings. Clinically there were diffuse cervical and in one case also axillary lympho-glandular enlargements, retrosternal dullness, and intermittent pyrexia with evening rises to 100–102° F. (37.8–38.9° C.). There were a moderate or severe hypochromic anaemia, a slight leucocytosis of 10,000 to 12,000 with a relative polymorphonuclear preponderance, and a B.S.R. between 60 and 70 mm. in one hour. One case had thin purulent left pleural and peritoneal effusions, and necropsy showed many tiny subpleural tubercles. The salient post-mortem findings were diffuse enlargement with gross caseation, but no liquefaction, of broncho-mediastinal, cervical, abdominal, and possibly also axillary lymphatic glands, gross miliary tuberculosis of the lungs, and miliary tubercles in the spleen, and in one case also in the liver. Two cases showed coincident portal cirrhosis with splenic and hepatic enlargement.

Type 5

The one case of this type, that of a man aged 50, may represent a modification of type 4, but certain differences were apparent. The case had proved puzzling owing to an associated maculo-anaesthetic leprosy. At necropsy both lungs were riddled with tuberculous bronchopneumonia. Near the left apex was a caseous lesion 1 by ½ in. (2.5 by 1.25 cm.), subpleural, without macroscopic limiting fibrosis but with an old overlying pleural adhesion. This was reported by the pathologist as "not a chronic lesion, but presumably the primary lesion of the recent infection, the pre-existing pleural adhesion being the determining factor of its site." Within one or two inches of this lesion were several zones of anthracosis and two small pinhead caseous foci reported as showing central scarring. The hilar glands were a little enlarged and contained caseous foci, and one, on section, was reported as "an old caseous encapsulated focus with some more recent tubercles." The more proximal broncho-mediastinal glands and the para-aortic glands in the abdomen were enlarged in lumpy masses, caseous and with liquefaction; splenic, pyloric, hepatic, and cystic glands were all moderately enlarged and grossly caseous. Cervical and axillary glands were greatly enlarged and confluent, and showed caseation and liquefaction. There was one tuberculous ileal ulcer, and the spleen and kidneys contained miliary tubercles.

Discussion and Conclusions

It is apparent that infection with the tubercle bacillus is now widespread, at any rate in the more populous areas of Nigeria, the primary infection being incurred usually in childhood or adolescence.

Progressive pulmonary lesions are rarely encountered in subjects under 17 years of age. It is recognized that such lesions can develop only if and when the lungs have acquired a high degree of sensitization to the products of the tubercle bacillus. It is thus evident that such allergy is not as a rule fully developed till after the age of approximately 17 years. The allergy responsible for the exhibition of a positive skin test, which is acquired as early as three months after the primary infection, must thus represent but one aspect of the process of sensitization. It seems that the attainment of sensitization to certain other fractions of the tubercle bacillus must extend over a period of years, its rate and degree varying possibly with the age incidence or dose of the primary infection or, more probably, with the number and frequency of early reinfections.

Further, the prevalence of tuberculosis of particular systems at particular age periods suggests that the various systems and tissues may attain maximum allergy at differing intervals from the primary infection. As an instance tuberculous adenitis in the European is most commonly seen in childhood, and is usually explained as a separate entity by postulating a distinct tonsillar or pharyngeal portal of entry, the result of a tendency on the part of young children to carry everything to their mouths. In the Nigerian I have most frequently encountered the disease among adolescents and young adults, while milk and milk products form no part of the dietary of the Southern Nigerian.

Though the communal eating-pot may provide a possible means of infection by ingestion, it seems equally possible that tubercle bacilli, entering by the usual method of inhalation of dust or droplets, may reach the cervical glands by lymphatic channels from the previously infected broncho-mediastinal glands. They there remain latent till later attainment of full allergy by the lympho-glandular system, possibly with the added precipitating factor of an intercurrent non-tuberculous infection of teeth, tonsils, or pharynx causes the appearance of manifest cervical glandular lesions. It is thus suggested that glandular tuberculosis should be regarded, like pulmonary tuberculosis, as a possible milestone on the path of any tuberculous infection, and not necessarily as a separately determined entity, and that every subject of a primary infection subsequently, over a period of years, passes through a stage of lympho-glandular sensitization, a later stage of pulmonary sensitization, and a final stage of desensitization.

Despite the extreme virulence of pulmonary tuberculosis in the African, the vast majority, although exposed to tuberculous infection, do not develop cavitative lesions. Further, the disease is not exceptionally prevalent among the African nursing staffs of medical wards—an observation consistent with the relative infrequency of the disease among European sanatorium staffs and the marital partners of open cases. The possible inference that the majority of such adults have attained to a state of desensitization does not seem probable, for they fall within the age period at which clinical phthisis is most frequent and therefore pulmonary allergy presumably maximal. It seems more likely that they have been predestined by early reinfections, either very infrequent or of small dosage, to a low subthreshold peak allergy, the course of which later adult reinfections are powerless to influence.

The typical phthisis of the European, with its features of fibrosis and chronicity, is not encountered in the African. The counterpart in the Nigerian—the type 1 group described above—is a rapidly fatal cavitative disease in which rapid weight loss, high pyrexia, concurrent caseous pneumonic lesions, absence of fibrosis, and often a leucocytosis with

polymorphonuclear preponderance all indicate a far more acute process and an inherent failure on the part of the African to develop a degree of immunity comparable to that of the European. The absence of glandular lesions indicates that the lympho-glandular system has passed the stage of maximum allergy and is now desensitized, while the absence of miliary lesions implies some degree of general immunity.

The type 2 cases differ in showing a somewhat earlier age incidence, a rather shorter duration of life, pulmonary lesions of a preponderantly caseous pneumonic type, and more or less widespread lympho-glandular caseation and miliary lesions elsewhere. It is suggested that development of allergy has been more rapid, so that the glandular system is still in a state of sensitization when the lungs prematurely attain their full allergy, and any general immunity is of very low degree.

Should lymphoglandular sensitization be extremely rapid and of high degree the patient may succumb, as in the type 4 cases, to a generalized glandular caseous tuberculosis with miliary spread. The lungs, being still unsensitized, show no gross lesions other than miliary. The African's susceptibility to the type 2 and type 4 forms of disease implies a propensity on his part to the development of an unusually high degree of allergy.

Pulmonary reinfections occurring before the establishment of full pulmonary allergy might be expected to produce lesions essentially of the primary type characterized by localized caseation without liquefaction or cavitation, but possibly more extensive and, as some degree of immunity has been acquired, with more evident localizing fibrosis. The type 3 case probably illustrates this kind of lesion.

Summary

The characteristics of pulmonary tuberculosis in the African have been discussed, and certain conclusions suggested regarding the course of this disease, in the light of Mantoux tests carried out on 229 subjects, a search for latent and healed tuberculous foci in 90 consecutive routine necropsies, and an analysis of the clinical and post-mortem findings in 36 consecutive cases of tuberculosis showing pulmonary lesions.

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The Twenty-sixth Report of the Investigation of Atmospheric Pollution covering the five years ended March 31, 1944, has recently been issued by the Department of Scientific and Industrial Research (London: H.M.S.O. Price 2s. 6d.). During the war the restrictions on emitting pollution were partly relaxed, and for a period industrial concerns were encouraged to make smoke for camouflage purposes. Despite this, the records of this nation-wide investigation show no appreciable increase of smoke in the air of the country as a whole, though an increase in the deposition of ash has been observed. The main reason for local improvements in atmospheric pollution was fuel economy. In rural areas the effect of ploughing grassland and of intensive cultivation was to increase the tendency for wind-blown dust to be collected in deposit gauges. The invisible pollution of the atmosphere by sulphur gases is almost directly proportional to the quantity of coal burned, irrespective of the size or type of the combustion appliance used, and from the summer of 1940 onwards the rapid increase in the consumption of coal due to great industrial activity caused an inevitable rise in sulphur dioxide pollution.

MYOIDEMA

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Myoidema was first described in 1830 by Robert Graves and William Stokes, of Dublin. When they percussed the chest they noticed that "a number of little tumours appeared answering exactly to the number and situation of the points of the fingers." They did not regard the phenomenon as peculiar to pulmonary tuberculosis. Cornet (1899), Denny-Brown and Pennybacker (1938), and Smart *et al.* (1948) mistakenly credit Schiff (1858) with priority in its discovery. Schiff made an elaborate physiological investigation of its occurrence in the lower animals. He described how "a localized knot of contraction immediately forms at the site of percussion and a series of small waves of contraction leave the knot on either side and travel to the ends of the muscle fibres, sometimes being reflected back again."

Tait (1872), a Birmingham surgeon who was presumably unfamiliar with Schiff's work, coined the word "myoidema." He separated the condition into two distinct components—the instantaneous formation of a sulcus, and the "nodule or intumescence of Stokes." He used the term for the nodular variety only, which he regarded as a significant sign of pulmonary tuberculosis. The sulcus formation, he said, may be "frequently met with in health." He agreed with the finding of Stokes that myoidema was more pronounced in the pectorals on the diseased side in unilateral pulmonary tuberculosis. Broadbent (1934) extended this observation further by pointing out that if both lungs were involved myoidema was more readily obtained on the more diseased side. In 12 cases of lung tuberculosis in our hospital, of which six were radiologically unilateral, we found myoidema to be equally marked in pectorals and biceps on the two sides.

West (1879) regarded the sign of little value in the diagnosis of any one disease, as it frequently occurred in a wide variety of conditions, and might be physiological. He thought the two kinds of contraction—the nodular and the fascicular—need not necessarily be associated, and that the term "myoidema" was not accurate as there was no oedema at all. He also pointed out the importance of subcutaneous fat in the production of the sign. The findings of Labbé (1881), Klippel (1903), Jeanselme and Lermoyez (1885), Curschmann (1905), Shively (1905), and Langley and Hashimoto (1918–19) supported West in showing the sign to be non-specific.

Féré and Papin (1901) drew attention to the presence of myoidema in the muscles of fatigued cyclists, of epileptics following a fit, and in muscles undergoing atrophy in general illnesses, general paralysis, and mental deficiency. They concluded that myoidema was a sign of muscular fatigue from any cause. Ebbecke (1935) considered the swelling of myoidema to be similar in nature to cathodal swelling. Debenedetti (1930) believed that myoidema ceased to appear when the individual put on weight, and suggested that this finding may be of prognostic importance in pulmonary tuberculosis.

Most of the English textbooks do not distinguish the two distinct components of muscular irritability, and the local lump (termed variously knot, ridging, nodule, intumescence, or nodular contraction) for which the word

myoidema was originally coined is not even mentioned. The terms "muscular irritability" and "myoidema" are mistakenly used synonymously for the fascicular or linear contraction-bands produced by tapping the pectoralis major (Martin, 1946). This error may be one explanation of the sign's having lost favour.

In South Iraq in 1944–5 obvious myoidema was found in 82 cases of peripheral neuritis, and this led to a search for it in patients suffering from other diseases and in supposedly healthy soldiers on duty. A high percentage of the latter groups also demonstrated a marked degree of myoidema. We tentatively ascribed the sign to malnutrition, and in particular to thiamin deficiency.

Our first observations were made in 1944–5 at an Indian General hospital at Shaiba in the extreme climate of South Iraq. The local garrison consisted of Indian and British troops, but the former were in a large majority. In 1945–6 observations were made on British troops returning from South-east Asia and India, on men working in a troopship, and on Indian troops in Syria-Lebanon. The Indian soldiers consisted of two dietetic groups, the meat-eaters and the vegetarians; the vegetarians had never taken meat or eggs in their life, but otherwise the living, eating, and working conditions of the two groups were identical.

TABLE I.—*Distribution of Myoidema*

	Nationality	No. of Men Examined	No. of Cases of Myoidema				
			Severe	Less Severe	Moderate	Slight	Absent
Hospital patients in S. Iraq (1944)	Indian M.	1,075	817	73	145	35	5
	„ V.	320	260	20	29	8	3
		1,395	1,077	93	174	43	8
Men on duty in S. Iraq (1944)	Indian	409	270	50	70	13	6
	British	176	31	30	50	32	33
	Chinese	109	64	14	20	11	0
Men returning from India and S.E. Asia (troopship, 1945)	British	124	19	27	21	17	40
	Waiters and cooks	34	20	8	2	2	2
	Lascars—stokers	39	22	11	3	2	1
	Deck-hands	42	13	11	6	5	7
Hospital patients, Syria-Lebanon (1945–6)	Indian M.	410	146	84	64	104	12
	„ V.	51	25	8	10	5	3
		461	171	92	74	109	15
Men on duty in Syria-Lebanon (1945–6)	Indian M.	352	156	72	48	52	24
	„ V.	72	36	10	13	10	3
		424	192	82	61	62	27

M = Meat eaters. V = Vegetarians.

Table I shows the distribution of cases of myoidema. It demonstrates: (1) Indian troops on duty had a degree of myoidema less than those sick in hospital; (2) meat-eaters often showed a lesser degree of myoidema than vegetarians; (3) British troops had a lower incidence of myoidema than all the other groups examined; and (4) Indian men on duty and in hospital in Syria-Lebanon had a lower incidence of myoidema than their counterparts in Iraq.

Technique of Elicitation

The patient held the forearm extended by the side of the body with the muscles relaxed. The belly of the right biceps was strongly pinched between the observer's thumb and forefinger, letting the muscle slide between them. A constant maximum strength of stimulus was aimed at. Myoidema was considered to be absent if the lump subsided before it could be palpated.

Myoidema could be elicited in all skeletal muscles, though in small and deeply placed muscles, especially if they were covered with strong fascia and fat, the sign was difficult to see and had to be palpated. Tapping with the fingers or a patellar hammer, as well as squeezing, elicited myoidema. The stimulated fibres momentarily contracted as a whole as the lump appeared. There were thus two components: the sustained lump at the site of the stimulus, and the flickering contraction of the whole length of the muscle fibres that preceded it. In patients with little subcutaneous fat a wave of contraction started at the lump in the pectoralis major and spread in both directions along the course of the fibres. In a few of these patients the wave appeared to return from the periphery to the site of the stimulus, possibly owing to the earlier subsidence of the peripheral contraction. The muscles which showed marked myoidema were often tender and the squeezing was painful.

Myoidema was not influenced by general anaesthesia or by spinal and nerve-block analgesia. It was therefore not a reflex but a direct response to a mechanical stimulus.

Myoidema in Neuritis

Severe myoidema was present in each of the 82 cases studied. In the 51 patients treated with thiamin it decreased in intensity in all except one, who was receiving anti-syphilitic arsenical injections at the same time as the thiamin. The decrease was gradual, and was obvious after about two months' treatment. There was no constant decrease in controls receiving hospital diet and cod-liver oil but not thiamin injections. Patients with neuritis who had recovered after two to three months' treatment with thiamin were discharged to duty. In these patients the myoidema had decreased or completely disappeared. Two cases relapsed after two months' duty. Myoidema was pronounced in wasting muscles, but not in those severely wasted. It was not more obvious in the muscles affected by neuritis.

Myoidema and Vitamin Deficiency

Deficiency of vitamin B (and possibly of vitamin A) was often seen in troops under our care (Table II). The presence or absence of these deficiency signs and of

TABLE II.—*Incidence of Vitamin Deficiencies*

	Nationality	No. of Men Examined	No. of Cases				
			Angular Stomatitis	Bitot's Spots*	Cheilosis	Generalized Glossitis	Geographical Tongue
Hospital patients in S. Iraq (1944)	Indian M.	1,448	1,108	85	1,218	11	62
	„ V.	415	325	18	329	9	13
		1,863	1,433	103	1,547	20	75
Men on duty in S. Iraq (1944)	Indian	409	362	15	465	2	8
	British	176	58	—	82	1	13
	Chinese	109	98	—	99	—	—
Hospital patients, Syria - Lebanon (1945–6)	Indian M.	410	186	7	114	—	5
	„ V.	51	23	5	19	—	3
		461	209	12	133	—	8
Men on duty in Syria - Lebanon (1945–6)	Indian M.	352	129	13	50	—	5
	„ V.	72	21	3	3	—	2
		424	150	16	53	—	7

* The relation of Bitot's spots to vitamin A deficiency is not established.

myoidema was recorded at the same examination, except for the troopship population, in whom myoidema only was looked for.

Analysis of the incidence of vitamin deficiency signs showed: (1) Indian troops on duty in Syria-Lebanon had a lower incidence of deficiency signs than those in hospital; this was not so in Iraq. (2) The meat-eating patients in hospital (Syria-Lebanon) showed a lower incidence of deficiency signs than vegetarian patients. (3) The British troops had a lower incidence of deficiency signs than the Indian troops. (4) Indian troops and hospital patients in Syria-Lebanon had a lower incidence of deficiency signs than those in Iraq: the hospital patients in Syria-Lebanon showed a lower incidence than men on duty in Iraq. These findings suggested that severe myoidema and vitamin deficiency were possibly related.

Myoidema and Chest Pain

The commonest complaints of medical out-patients in our general hospital in Iraq in 1944 were pain on each side of the chest and loss of appetite, general weakness, and general aches and pains. Men with these complaints often had painful severe myoidema and active tendon-jerks. Some patients complained of giddiness, and others of cramps in the calf muscles and sciatic pain. Scores of such men were seen at the end of the hot weather, and were sent to hospital with such diagnoses as myalgia of the chest, neuralgia, fibrositis, pleurodynia, pleurisy, and sciatica. Many were sent for investigation of supposed early tuberculosis or cardiac disease and were unnecessarily submitted to *x*-ray and other examinations. Some were given procaine injections for supposed fibrositis.

Chest pain was the commonest single symptom, and was complained of as a constant diffuse ache on both sides of the chest. This pain usually disappeared after thiamin injections had been given for 10 to 20 days, or after longer periods if yeast tablets were taken. The frequency with which pain in the chest responded to thiamin was striking, but under field conditions a controlled experiment was not possible. It was thought that this pain was associated with fatigue of the chest muscles, which were presumably in an early pathological condition, as shown by severe myoidema. Patients recovered when thiamin was given. Many of these patients were seen by a psychiatrist, because the symptoms were often excessive fatigue, exhaustion, and depression, but in most cases no psychiatric abnormality was found. The same symptoms, however, were often absent in men on duty who were found to have severe myoidema. We had the impression that the incidence of severe myoidema was greater at the end of the hot weather. Routine urine examinations showed no salt depletion.

Cause of Myoidema

Kollert and John (1925) reported that 40% intravenous glucose abolished or diminished myoidema; they suggested that the sign was related to failing carbohydrate metabolism. The addition of insulin increased the effect of intravenous glucose. John and Dattner (1926) considered that in a number of conditions producing vasomotor disturbance myoidema was always present, and the capillaries in these patients showed thickening, tortuosity, and absence of contractility. They thought that intravenous glucose improved the contraction of capillary walls, increased the blood flow, and brought about disappearance of myoidema. Grill (1927) found that a large number of patients showing myoidema had raised lactic acid levels in the blood.

Koumans (1928) reported myoidema to be a common finding in poor-class Javanese, Malays, and Chinese in the Tropics. Their well-to-do counterparts and the Europeans, even after a long stay in the Tropics, did not show myoidema. He found it had no relationship to any disease, to overexertion, to the blood-sugar level, or to deficient carbohydrate intake, but was related to unbalanced diet and undernutrition. He regarded myoidema as a sign of avitaminosis. John (1928), criticizing Koumans's paper, stated that myoidema did occur in cases showing no avitaminosis. Seto (1937), working in Japan, confirmed Koumans's findings.

Denny-Brown and Pennybacker (1938) made electromyographic studies of two cases showing myoidema and, citing the work of Gelfan and Bishop (1932, 1933) and Gelfan (1933–4), were of the opinion that the phenomenon was due to a disturbance of the excitability of muscle fibre, predominantly of its contractile contents. They postulated a disturbance of the potassium : sodium ratio and the raising of excitability of both sarcolemma and muscle fibre. These workers were of the opinion that in a normal muscle percussion induced a "small knot of contraction with tightening of the remainder of the fasciculus," and that both subsided in one to five seconds, according to the intensity of the stimulus. If the local contraction lasted more than 10 seconds they regarded it as abnormal. Smart and his collaborators (1948), studying Belgian workers who were receiving inadequate food, found the biceps "ridge" lasted longer in them than in healthy R.A.F. personnel (about 4.5 seconds and 2.1 seconds respectively), but the phenomenon decreased in duration after food supplements had been given. They could not indicate which biochemical lesion produced the hyperirritability.

Analysis of the association of severe myoidema with coincident illness, dietetic habit, and vitamin deficiency suggested that in our cases the sign denoted malnutrition. The evidence for associating myoidema with disordered thiamin metabolism was that in 51 cases of neuritis treated with thiamin myoidema decreased and in many cases disappeared. Thiamin also cured the associated chest pain and muscular tenderness. The part played by thiamin, however, may have been an indirect one, by restoring the appetite.

Under certain conditions severe myoidema may be a pre-neuritic phenomenon. Peripheral neuritis was common in our garrison, and all the cases had severe myoidema. The incidence of severe myoidema among troops on duty was also high: they often had tender muscles, pain in the chest and calf muscles, cramps, and exaggerated tendon-jerks, like those seen in early cases of neuritis in our series.

Since the men's rations were stated to contain normal quantities of thiamin (3 mg. daily) other causes for disordered thiamin metabolism were considered. Thiamin deficiency may have been due to loss of appetite, to diarrhoea, and to loss in sweat (especially during the hot weather, when sweat loss amounted to over 10 pints (5.7 litres) daily). An attack of fever, or extra marching, may have precipitated thiamin deficiency by increasing thiamin requirements.

Summary

Severe myoidema was found in South Iraq in a series of cases of peripheral neuritis in soldiers on duty and in patients suffering from other diseases.

The condition was related to the nutritional state and the dietetic habit of the groups of men examined. It accompanied signs of vitamin deficiency, and disappeared when the cases of peripheral neuritis were treated with thiamin. It is suggested

that in our cases severe myoidema was a sign of malnutrition and was probably related to thiamin metabolism.

An explanation is attempted of the growing disrepute of myoidema as a physical sign.

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LYMPHADENOPATHY IN BRUCELLOSIS

BY

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Lymphadenopathy is not a prominent feature of brucellosis. Most of the textbook articles on the subject make no mention of the lymph nodes. Bloomfield (1942) made an extensive survey of published case reports in an attempt to discover if specific lymphadenopathy ever occurs in Brucella infections. He found that most authors omitted all reference to the nodes, and detailed information was difficult to obtain. He concluded, however, that noteworthy enlargement of the superficial glands was not uncommon, although its significance was seldom clear because the available data on the clinical course of the adenitis in relation to the progress and outcome of the disease were usually inadequate.

In view of the confusion, it was decided to make a careful clinical examination of the lymph nodes in patients suffering from melitensis fever in a military hospital in Malta. The series consisted of 42 cases, all the patients being under observation in hospital throughout the course of their illness. In 30 the diagnosis was proved by blood culture; in 11 repeated blood cultures were negative, but melitensis agglutinins were present in the sera in titres varying from 1 in 1,280 to 1 in 20,480; in the remaining case blood cultures and agglutination tests were negative and the diagnosis was made on purely clinical grounds. Generalized superficial lymphadenopathy was an outstanding initial feature in two patients, and in both instances caused difficulty in diagnosis. The other 40 cases were entirely free from lymph-node involvement during their stay in hospital.

Case 1

A Maltese man aged 21 was admitted to hospital on December 3, 1945, with a provisional diagnosis of glandular fever. His complaint was of headache, anorexia, and shivering attacks for five days. He looked very ill and his temperature was 102.4° F. (39.1° C.). There was bilateral and symmetrical enlargement of the cervical (anterior and posterior), axillary, epitrochlear, and inguinal lymphatic glands. The glands were mobile, discrete, firm, and non-tender, and varied in size from 1 to 2 cm. in diameter. The throat was clean. There was no enlargement of the liver or spleen. The leucocyte count was 6,850 per c.mm. (polymorphs 20%, lymphocytes 51%, monocytes 29%—a fair proportion of the latter resembled "glandular-fever cells"). The Paul–Bunnell test was positive in a titre of 1 in 32.

In the first few days the temperature intermitted between 104° F. (40° C.) and normal; the patient had several rigors and severe epistaxis occurred on three occasions. He complained bitterly of neuralgic pains in his arms and legs. The cerebrospinal fluid was normal. An initial diagnosis of glandular fever was made, but six days after admission his serum agglutinated *Br. melitensis* in a titre of 1 in 10,240. Blood culture was performed on the same day, and after 14 days' incubation a profuse growth of *Br. melitensis* was obtained. A radiograph of the chest showed no enlargement of the mediastinal glands. The acute symptoms subsided slowly and the temperature fell by lysis after remaining high for 10 days.

The subsequent course was typical of that pursued by a severe case of undulant fever—recurring bouts of fever, progressive anaemia, and flitting arthritis. The glands decreased in size very slowly, and by the end of the sixth week none were palpable. The Paul–Bunnell test was repeated twice and remained positive in the same titre (1 in 32). In the sixth week the leucocyte count was 6,700 per c.mm. (polymorphs 45%, lymphocytes 43%, monocytes 12%). The patient was discharged at the end of the third month, when he had been afebrile for three weeks.

Comment.—The enlargement of the glands, the blood picture, and the epistaxis were considered sufficient evidence, in the beginning, to allow a diagnosis of glandular fever. The titre of the Paul–Bunnell test was, however, not of diagnostic value. The melitensis infection was discovered subsequently only because local experience had taught the value of performing the appropriate bacteriological tests in all febrile patients in whom there was the slightest doubt about the diagnosis.

Case 2

A Maltese man aged 25 was admitted to hospital on June 3, 1946, with a provisional diagnosis of leukaemia. He had been ill for several weeks, and complained of vague febrile symptoms, weakness, and swellings of the neck. He was not severely ill and his temperature was 100° F. (37.8° C.). He looked pale but well nourished. The cervical, supraclavicular, epitrochlear, axillary, and inguinal glands were enlarged on both sides. They were firm, discrete, mobile, and non-tender, and were largest in the neck and axillae, where they measured up to 2 cm. in diameter. The tip of the spleen was palpable on deep inspiration but the liver was not enlarged. The blood picture was as follows: Hb, 70%; red cells, 3,650,000 per c.mm.; white cells 5,200 per c.mm. (polymorphs 45%, lymphocytes 45%, monocytes 10%—no abnormal cells present). The Paul–Bunnell test was negative. Low-grade fever continued and a tentative diagnosis of Hodgkin's disease was made.

A gland biopsy was arranged, but on the fifth day, before it was carried out, he had a rigor with high fever. At this time blood was taken for culture and the melitensis agglutination test. The latter was positive in a titre of 1 in 20,480, and after 17 days' incubation a profuse growth of *Br. melitensis* was obtained in the culture medium. During the next six weeks

there were three waves of fever before the temperature settled. The glands did not alter for two weeks; they then slowly decreased in size, and on discharge at the end of the ninth week only a few small nodes were palpable in the left posterior cervical triangle. At this time the spleen was not enlarged. Mild arthritis of the left knee developed but was not troublesome. Treatment was symptomatic.

Comment.—The anaemia, fever, lymphadenopathy, and splenomegaly suggested Hodgkin's disease. At first a diagnosis of brucellosis was not considered, and the melitensis infection was discovered, as in the previous case, by the application of routine tests.

Discussion

Conflicting statements appear in the literature about lymph-node involvement in brucellosis. McArthur (1939), in an important survey of the subject, made no reference to lymph glands. Musser (1938, quoted by Bloomfield, 1942) stated that general lymph-node swelling did not occur. On the other hand, Menefee and Poston (1938) found that lymphadenitis was often present. Avery (1942) noted that the glands were occasionally enlarged—either the cervical group alone or generalized.

Bloomfield (1942) consulted 191 unselected case reports and found specific mention of the lymph nodes in only 50—29 with enlargement and 21 without. In the 29 positive cases the distribution was as follows: cervical only, 13; generalized (superficial), 9; axillary only, 3; cervical and inguinal, 3; axillary and inguinal, 1.

As Bloomfield pointed out, the enlargement in many cases may have been merely incidental and not a specific manifestation of brucellosis. He was particularly doubtful about the cases with only localized involvement. In seeking evidence for the existence of a specific lymphadenopathy the important patients for scrutiny would seem to be those with generalized adenitis. This group consisted of nine cases, and further information about the glands during the course of the disease was given in only three. In one the swellings subsided about the fifth week and in another they persisted until the tenth month, when observation ended. The symptoms regressed rapidly in the third case and the glands decreased in size within three days of admission; biopsy showed chronic lymphadenitis with necrotic foci, and *Br. suis* was isolated from the excised node. This patient died after multiple relapses, and the necropsy revealed generalized lymphadenitis of no specific histological type. *Br. suis* was recovered from many sites, including the lymph nodes. Gland biopsies were performed in two other patients; the lesion in one was "inflammatory," and the other served to exclude Hodgkin's disease and leukaemia.

Bloomfield concluded from his analysis of the nine patients with generalized adenitis that the lesion was probably specific for brucellosis in five, possibly in two, and of doubtful significance in two. No special aetiological importance could be attached to any single variety of Brucella—all three (*melitensis, abortus, suis*) were incriminated. Bloomfield added a case of his own which had enlargement of axillary, inguinal, and epitrochlear glands. Biopsy resulted in a histological diagnosis of lymphatic leukaemia, but the patient improved rapidly without therapy and the glands disappeared in the course of a year.

The generalized lymphadenopathy in both cases described above was without doubt a specific manifestation of brucellosis, the proof being the disappearance of the swellings as the general condition of the patients improved. Its occurrence in only two out of 42 cases suggests that it is not common.

The importance of the occasional occurrence of lymphadenitis in brucellosis is the confusion that it may cause in diagnosis. This point is well demonstrated by both of my cases. In Case 1 the clinical diagnosis of glandular fever seemed to be confirmed by the haematological examination. Wise (1943) drew attention to the fact that the study of the leucocytes in brucellosis frequently reveals abnormal cells suggestive of the early stage of glandular fever. Leys (1943) had two cases of abortus fever in which the monocyte count was so high that mononucleosis was considered as a possible diagnosis.

Rubenstein and Shaw (1944) stressed the clinical similarity which often exists between brucellosis and glandular fever. They pointed out that glandular enlargement was strongly in favour of the latter. Case 2 shows a superficial resemblance to Hodgkin's disease. Anaemia, splenomegaly, and lymphadenopathy may be common to both brucellosis and lymphadenoma, and the resemblance may be even closer in those cases of the latter which are characterized by the Pel-Ebstein type of fever. Parsons and Poston (1939) were of the opinion that in some cases of brucellosis even the histology of the lymph nodes may suggest Hodgkin's disease.

It is apparent that great advances are being made towards the goal of specific therapy for brucellosis (Spink, Hall, Schaffer, and Braude, 1949; Herrell and Barber, 1949). With the discovery of effective chemotherapeutic and antibiotic agents early diagnosis, previously of little moment, takes on a new importance. In such a protean disease diagnosis is notoriously difficult and clinical suspicion requires bacteriological confirmation. Mistakes arise when the physician, faced with a case of obscure pyrexia, does not suspect brucellosis. In areas where the disease is not common the error may be one of simple omission; but occasionally, as in the cases described above, the presence of an unusual clinical feature may cause such close resemblance to other conditions that the true diagnosis is obscured unless the specific bacteriological tests are employed. An awareness of the specific lymphadenopathy of brucellosis may prevent cases being wrongly diagnosed as glandular fever, lymphadenoma, or even leukaemia. A serious prognostic error may therefore be avoided and adequate therapy will not be withheld.

Summary

Two cases of melitensis fever in which generalized lymphadenopathy was a prominent feature are described. One case closely resembled glandular fever and the other simulated Hodgkin's disease.

The occurrence of specific lymphadenopathy in brucellosis is discussed and the difficulty in diagnosis which it may cause is stressed.

Lack of knowledge of this cause of lymphadenopathy may result in a serious prognostic error, and by delaying diagnosis may prevent the use of therapeutic measures at their most effective stage.

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CLINICAL TRIALS OF SUCCINATES AND OF HEPARIN IN RHEUMATIC FEVER

BY

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The use of salicylates in the treatment of rheumatic fever is traditional. The therapeutic employment of this class of substances followed work originally described by Maclagan (1876). Many theories have been put forward to explain the action of salicylates, but no one has advanced a really tenable hypothesis. The subject has been reviewed and discussed from the biochemical, enzymatic, and clinical points of view by various authors (Glazebrook and Cookson, 1947; Wrigley, 1948).

Advances in the treatment of rheumatic fever have been concerned mainly with the dosage and route of administration of salicylates. It was with great interest, therefore, that we read of the work of Gubner and Szucs (1945), who drew attention to the therapeutic possibilities of succinates. Succinates act as catalysts in biological oxidation—for instance, in the metabolism of carbohydrates (Krebs, 1943) and of fatty acids (Breusch, 1943; Muñoz and Leloir, 1943). Gubner and Szucs suggest that during rheumatic fever there is an inactivation of various enzymes, and that the administration of succinates may prevent the inhibition of succinic dehydrogenase (cytochrome C reductase) and the inactivation of other respiratory enzymes. The administration of ascorbic acid and the use of the calcium salt of the succinate also seem to be indicated, because ascorbic acid and calcium enhance the activity of succinic dehydrogenase.

Gubner and Szucs's Results

Gubner and Szucs tested their theory by treating cases of rheumatic fever with sodium salicylate and sodium bicarbonate, sodium salicylate and ascorbic acid, sodium bicarbonate alone, sulphathiazole, penicillin, and calcium double salt of benzoic acid and succinic acid benzyl ester plus ascorbic acid. They found that penicillin, sulphathiazole, and sodium bicarbonate were useless, and that treatment with any one of them alone had to be discontinued after a few days because of the increased severity of the disease. A comparison of the cases treated by them with salicylates and with the succinate compound is given in Table I.

TABLE I.—*Comparison of the Therapeutic Effects of Salicylates and Succinate (Gubner and Szucs)*

	Tyoe of Therapy	
	Salicylates (4·5 g. Daily)	Succinate (Average Dose 4·2 g. Daily). Ascorbic Acid (200 mg. Daily)
Total No. of cases	65	55
Period in hospital	52 days	34 days
Period on drug therapy	48 "	27 "
Incidence of drug toxicity	19%	2%
Duration of fever	13·5 days	5·7 days
Duration of leucocytosis	22 "	14 "
Duration of accelerated B.S.R.	43 "	24 "
Incidence of carditis	69%	19%
Incidence of relapse	7%	0%

No toxic symptoms were observed in the cases receiving succinate, except for flushing and slight mental confusion in one patient, and occasional nausea. Evidence accepted as indicating carditis included murmurs, gallop rhythm, pericarditis, and *x*-ray and electrocardiographic abnormalities. The figures indicate that the succinate compound is of considerable benefit and constitutes a great advance in the treatment of acute rheumatism.

Extension of this work was carried out by Szucs (1947), using a mixture of calcium salicylate and aspirin. The results claimed by him are shown in Table II.

TABLE II *(Szucs's Results)*

Type of Case	No. of Cases	Result
Osteoarthritis	208	Definite improvement in 95% within eight days
Acute infectious arthritis	17	All evidence of arthritic activity disappeared within ten days
Rheumatoid arthritis	27	22 cases showed definite improvement, with arrest of arthritic activity within an average of three months
Mixed arthritis	15	8 cases showed marked improvement, with complete or almost complete cessation of arthritic activity within an average of two months
Spondylitis	95	Improvement of variable degree in the majority
Rheumatic polyarthritis	34	All evidence of rheumatic activity disappeared within an average of 14 days

Most of the cases of rheumatoid arthritis were said to have previously received an adequate course of gold without definite improvement.

Present Investigation

In view of these published results we think it of interest to record our experiences in the treatment of acute rheumatic fever with: (*a*) calcium monobenzyl succinate, 10 gr. (0.65 g.) four-hourly, omitting night dose = 50 gr. (3.25 g.) daily; and (*b*) calcium double salt of benzoic acid and succinic acid benzyl ester, 10 gr. four-hourly, omitting night dose = 50 gr. daily; together with 200 mg. of ascorbic acid daily.

The calcium double salt of benzoic acid and succinic acid ester, together with ascorbic acid, was used to test the validity of the earlier claims of Gubner and Szucs, and their dosage recommendations were adopted. Calcium monobenzyl succinate was used because it presented a different form of the same essentials and might have been instructive from the point of view of treatment.

Anticoagulants

Glazebrook and Cookson (1947) have pointed out that substances benefiting acute rheumatic fever, rheumatoid arthritis, and anaphylactic states have a common action in that they are all anticoagulants—namely, salicylates in rheumatic fever, deep jaundice in rheumatoid arthritis, and heparin in anaphylactic states. On this basis they built up a theory that the curative effect of salicylate in rheumatic fever depended upon its power to prevent protoplasmic clotting and cell death precipitated by the irritation of intracellular antigen–antibody reactions.

This explanation of salicylate action rests on the unproved assumptions that rheumatic fever is a manifestation of allergy, and that protoplasmic clotting is the same process as blood-clotting and can be inhibited by the same anticoagulants. There is reason to suppose that Heilbrunn's (1943) work, showing a similarity between the mechanism of blood-clotting and of protoplasmic clotting, is not securely founded (Cookson, 1947—personal communication), while the hyaluronidase story of rheumatic fever (Guerra, 1946) is claiming increasing attention. However, these developments do not detract from the importance of

the work of Glazebrook and Cookson in drawing attention to the anticoagulant group of drugs.

Heparin is an inhibitor and salicylates may be inhibitors of hyaluronidase, and from its chemical constitution dicoumarol would seem very likely to be an inhibitor of hyaluronidase. It seemed to us, therefore, that there was a strong case for the use of heparin in acute rheumatic fever, and that good results might be expected because of either its anticoagulant properties or its inhibiting effect on the spreading factor, hyaluronidase. Wassen and Zander (1946) have reported good clinical results from the treatment of rheumatoid arthritis and of rheumatic fever with heparin and dicoumarol, and we have also recorded our experiences in the treatment of acute rheumatic fever with heparin (1,000 T.U. intravenously thrice daily) and salicylates (200 gr. (13 g.) daily in four-hourly doses). A control group was given salicylates, without heparin, and all three groups were also given 200 mg. of ascorbic acid daily. The results are set out in Table III.

TABLE III.—*Details of Cases Investigated*

Case No.	Sex	Age	Previous Attacks	Duration of Illness before Admission (Days)	Evidence of Carditis on Admission	No. of Joints Affected	Maximum Temperature °F.	Maximum Temperature °C.	Maximum B.S.R.	Duration of (Days) Joint Pains	Duration of (Days) Pyrexia	Duration of (Days) Increased B.S.R.	Carditis on Follow-up	Succinate Used	Remarks
Succinate Group															
1	F	18	1	7	No	10	101	38·3	42	6	6	54	No	B	
2	F	19	0	6	Yes	8	102	38·9	102	18	23	51	,,	A+B	Pyrexia terminated by salicylate
3	F	18	0	21	,,	6	104	40	75	12	9	68	Yes	A	One relapse: total pyrexia, 12 days
4	M	40	1	21	,,	9	101·8	38·8	100	10	9	65	,,	A	Three relapses: total pyrexia 14 days. Pyrexia terminated by salicylates
5	F	29	1	2	,,	6	100·8	38·2	62	3	3	54	,,	B	
6	F	57	0	10	No	8	102	38·9	68	18	18	76	No	B	Pyrexia cut short by salicylates
7	M	24	0	21	Yes	6	101	38·3	65	34	38	77	,,	A	
8	M	15	0	1	,,	6	101	38·3	69	9	6	87	,,	A	
9	M	15	0	14	,,	4	99·8	37·7	48	3	3	62	Yes	A	
10	M	15	0	5	,,	11	99·8	37·7	85	3	7	61	,,	B	
										11·6	12·2	65·5	50%		
Heparin Group															
1	F	16	0	2	Yes	4	101	38·3	65	4	2	35	Yes		
2	F	19	0	7	,,	4	104	40	102	3	8	45	,,		
3	F	18	2	4	No	6	102·5	39·15	72	3	2	22	No		Two relapses with slight pyrexia
4	F	13	1	7	Yes	4	98·1	36·75	78	4	0	51	,,		
5	F	18	0	2	,,	6	102·5	39·15	76	5	5	98	Yes		
6	M	17	0	7	,,	10	99·8	37·7	80	4	2	61	No		
7	M	13	0	3	,,	4	102	38·9	80	7	4	78	Yes		Severe epistaxis; relapsed twice: total pyrexia 12 days
8	F	17	2	7	,,	6	103	39·4	134	4	2	51	,,		Relapsed twice: total pyrexia, 22 days
										4·2	3·1	55·1	62%		
Salicylate Group															
1	M	15	0	4	Yes	4	103·5	39·75	110	7	2	58	Yes		Relapsed: developed chorea, collapse of middle lobe and hyperpyrexia. Died after 26 days' further pyrexia
2	M	18	2	4	,,	6	100·5	38·05	80	4	6	58	,,		
3	M	46	1	20	,,	8	103·5	39·75	129	13	5	116	No		Pericarditis, pleurisy, three relapses: total pyrexia, 21 days
4	F	21	0	21	No	7	100	37·8	118	5	7	46	,,		
5	M	16	1	6	Yes	7	102·5	39·15	88	2	3	43	Yes		
6	F	16	0	7	No	8	103·5	39·75	92	6	6	35	No		
7	M	11	0	6	Yes	8	101·5	38·6	25	4	4	41	,,		
8	F	18	1	4	No	3	102·5	39·15	92	3	3	81	,,		Two relapses: total pyrexia, 10 days
9	F	34	0	10	Yes	13	103	39·4	122	2	7	37	Yes		
10	F	38	1	21	No	3	102	38·9	115	3	2	39	No		One slight "spike": total pyrexia, 4 days
										4·9	4·5	55·4	40%		

A = Calcium monobenzyl succinate, 10 gr. 4-hourly.
B = Calcium double salt of benzoic acid and succinic acid benzyl ester, 10 gr. 4-hourly.

Most of the columns are self-explanatory. With regard to the presence of carditis, all cases having any suggestion whatever of cardiac involvement—e.g., a mitral systolic murmur without *x*-ray or electrocardiographic evidence of abnormality or other physical sign—have been so classified. It is possible that this definition of carditis has been too strict, and that some of the cases so designated would make good recoveries.

Discussion

It can be said at once that neither form of succinate compound used in this trial represented any advance on salicylate therapy. The duration of joint pains, of pyrexia, and of elevation of the blood sedimentation rate was much longer than in the salicylate-treated group. What is more to the point, Case 2 in the succinate group had succinate A without improvement, and then succinate B also without improvement. Finally, salicylates had to be given to terminate the pyrexia. Two other cases (Nos. 4 and 6) also did badly on succinates and showed great improvement immediately they were switched to salicylates. Evidence of carditis on follow-up was present in 50% of the cases, as compared with 40% in the salicylate-treated group, but not much importance can be attached to this, as the majority of cases had evidence of carditis on admission, before treatment had started.

We have not been able, therefore, to find any support for the contention of Gubner and Szucs that succinates given without salicylates improve cases of acute rheumatism. It will be noticed that in the second series of cases treated by Szucs calcium succinate was used together with aspirin. This we think strange in view of the apparently good results

in the first series of cases treated by a succinate compound without aspirin.

The calcium double salt of benzoic acid and succinic acid benzyl ester has also been used for the treatment of rheumatic fever by Wégria *et al.* (1948). They conclude that neither the natural course of the disease nor its signs and symptoms were modified by succinate therapy.

The group treated with heparin was very little different from the salicylate group when the duration of joint pains, of increased pyrexia, and of increased blood sedimentation rate is considered, although it does seem that the duration of pyrexia was less in the cases given heparin. The presence of carditis on follow-up was found in 62% of the cases given heparin, but in only 40% of the cases given salicylates. Practically all of the cases in the heparin-treated group had carditis on admission, before treatment with heparin had begun, but they had been given salicylates outside by their own doctors before coming under observation. As in the case of the succinates, therefore, not much importance can be attached to this finding.

It would seem from these studies that we have not yet found anything which represents an advance in therapy in the treatment of rheumatic fever. Nevertheless, although succinates are certainly not effective, as are salicylates, in cutting short the pyrexia of an acute rheumatic episode, there has been offered no proof in this paper that they are not an adjuvant to salicylate therapy. Until some method of administering heparin is found which will maintain a constant blood level without the necessity for repeated intravenous injections, a really satisfying trial of this product cannot be made.

Conclusions

Succinate compounds given with ascorbic acid in the dosage recommended by Gubner and Szucs are ineffective in the treatment of acute rheumatism. Heparin, in a dosage of 1,000 T.U. three times daily, does not significantly reduce the duration of episodes of acute rheumatic fever treated with salicylates.

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Dr. G. R. Wendt, chairman of the Psychology Department of the University of Rochester, U.S.A., is recently reported to have said that because a serious amount of charlatanism has developed in the U.S.A. it is essential that all groups concerned with the mental health movement should collaborate to protect the public through legislation (*New York Times*, September 11, 1949). Dr. Wendt considers that it is the primary responsibility of the medical profession to take the initiative in working for the protection of the public. He decried the almost complete lack of mental health legislation in the U.S.A. despite the great need for it. Only in Kentucky is there a law making it mandatory for each psychologist to get a licence before he can conduct private practice.

SUBACUTE POISONING BY THALLIUM TREATED WITH BAL

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In our paper on a fatal case of subacute thalliotoxicosis (Mazzei, Schaposnik, and Pedace, 1948a) we emphasized the basic clinical characters of acute, subacute, and chronic poisoning by thallium, together with the micropathology of each. The present paper deals with another case of poisoning by thallium—a suicidal attempt—which was successfully treated with BAL.

Though there does not seem to be any clinical experience with this drug in this type of poisoning, we decided to try it. Afterwards, Furmanski (1948) explained the beneficial action of BAL in poisoning by thallium. He used the drug with favourable results in severe peripheral neuropathies which had proved intractable to large doses of vitamins and crude liver extract. He based the treatment on the accepted view that such neuropathies are caused by the inactivation of the enzymatic systems of the nerve cells by toxins or toxic metabolites. He thought that BAL acted in these cases in a similar way to that in metal poisoning—i.e., by combining itself with the toxic metabolites after setting free those enzymes vitally related to cell respiration.

With these facts in mind, we thought that in human cases of poisoning by thallium BAL could be of use by displacing and then eliminating the metal already combined with protein enzymes of the nervous cells.

Dosage and Toxic Disorders

In the light of Eagle's wide experience, the Council of Pharmacy and Chemistry of the American Medical Association suggests the following outline of dosage in arsenical poisoning; this outline can be extended to poisoning by other metals.

In severe arsenical reactions.—First and second day, six daily injections of the drug, each of 3 mg. per kg. of body weight. Third day, four injections of the same dose. During the following 10 days or until full recovery is attained, two daily injections.

In reactions of medium severity.—Each injection should consist of 2.5 mg. per kg. of body weight. During the first two days four doses should be given, two on the third day, and one during the following 10 days or until full recovery.

In our case we used approximately the medium-severity doses, the total amount of drug injected being 3.1 g.

The administration of BAL may give rise to some unpleasant though transient effects. In view of its affinity for heavy metals, some of the toxic disorders following the use of high doses can be attributed to its combination with the metals which form part of the molecule of certain enzymes (copper, zinc, iron, and manganese). The removal of the heavy metals renders inactive the corresponding enzymes by depriving them of their protein groups (Furmanski, 1948). This theory seems to be supported by the drop in the magnesium content of the blood and disruption of the calcium/magnesium balance seen in patients receiving BAL, thus giving rise to the characteristic

symptoms of tetany. However, the enzymatic inhibition is rapidly reversible, so the accident does not seem to have undue importance.

The most common toxic symptoms are excessive salivation, vomiting, lacrimation, sweating, generalized myalgias, headaches, severe fleeting pains at the site of the injection, tachycardia, increased blood pressure, dyspnoea, and precordial constriction.

We must call attention to the high levels of the blood pressure in our patient. Though thalliotoxicosis is often accompanied by high blood pressure—especially the diastolic—the rise was evidently coincident with the course of BAL; it must therefore be attributed, partly at least, to the action of the drug.

Case Report

The patient, an Argentine girl aged 16, was a student at a secondary school, and lived in La Plata, province of Buenos Aires. During the three days September 16–18, 1948, she swallowed approximately 34 g. of the rat-poison paste "zelio," which contains 2% of thallium sulphate. On September 20 she began to feel skin hyperaesthesia and pains in the muscles of her lower limbs. On the following day her temperature rose to 38° C. (100.4° F.) and the myalgias had become very severe. The mere touch of the bedclothes caused violent pains, and she became progressively unable to use her legs.

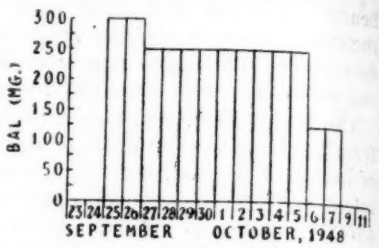
On September 20 one of us was called in to see her. The temperature was 40° C. (104° F.). She was restless, with facies dolorosa, of asthenic habitus, and was lying on her back because of severe pain in her feet and legs, which was greatly intensified by the slightest touch or movement. She was undernourished, with small amount of subcutaneous fat. Her skin was hot and dry. The shape and reflexes of the pupils were normal. Her pulse was rhythmic, 84 a minute; blood pressure 170/120 mm. Hg. On palpation the whole of the abdomen was tender. The liver and spleen were within normal limits; the renal areas were painful. She was completely unable to move her lower limbs, and passive mobilization caused intense pain, particularly in the feet. The severe hyperalgesia made it impossible to carry out a thorough examination. The Achilles-tendon, patellar, and abductor reflexes were increased.

A psychiatric examination was performed by Dr. Alejandro Resús, who reported: "Her mental picture is prior to her attempt at poisoning, and must be the determining factor of the same. The symptoms correspond to the development of a constitutional and atypical exacerbation, which is due to the overlapping of the emotional psychasthenic and schizoid components (hypermotivity, erythrophobia, exaggerated psychomotor reactions; varied neurotic tendencies, phobias, and certain obsessions; a tendency to introversion and isolation, ideo-affective disassociation of personality)."

Laboratory Tests.—Blood count: red cells, 4,789,000; Hb, 95%; platelets, 240,000; white cells, 6,400 (neutrophils 60%, eosinophils 0.66%, monocytes 13%). Coagulation time: five minutes; bleeding time: two minutes. Sedimentation rate: first hour, 15 mm.; second hour, 38 mm. Blood urea, 30 mg. per 100 ml.; blood sugar, 96 mg. per 100 ml; blood cholesterol, 180 mg. per 100 ml.; alkali reserve, 50 vols. %; chloride in cells, 1.56 mg. per 100 ml.; chloride in plasma, 264 mg. per 100 ml.; blood proteins, 8.28 g. per 100 ml. (serum albumin, 4.82 g.; serum globulin, 3.46 g.). Urine: turbid; acid reaction; slight sedimentation; specific gravity 1009; ammonia 0.47 g., urea 13.1 g., chlorides 2.2 g., phosphates 1.3 g., albumin 1.5 g. per litre; no sugar, acetone, or bile pigment. The sediment showed granular and hyaline casts, some red cells, and a large number of desquamation cells.

Treatment and Progress

On September 23 treatment was started with sedatives, analgesics, 25% glucose solution intravenously, vitamin B complex, and 15% magnesium sulphate with 0.05 g. of papaverine intramuscularly. Two days later the first phials of BAL from an English firm were obtained. During the first two days 300 mg. was injected daily. After this the treatment was continued with the same product, but of American origin (10% solution). A total of 3.1 g. was given (see Chart).



Throughout the administration of the drug the patient developed a morbilliform exanthema of varying degrees in the upper limbs, neck, and chest. Each injection of BAL gave rise to intense headaches and greatly increased the pains in the lower limbs; opiates were partially successful in alleviating these conditions. Weekly estimations of the urine showed considerable fluctuations in the albumin content (between 0.2 and 1.5 g.); albumin, together with renal elements, finally disappeared in February, 1949.

A few days after treatment was suspended the pains in the lower limbs began to decrease, and by December, 1948, the patient was free from them. The muscles of the thighs and legs gradually recovered their original tone and size with the help of massage. The hair on the head began to fall on October 5, and within a few days only a few patches of short hair remained.

For three months the patient was treated in a private mental institution. Insulin shock brought about a definite improvement in her psychic manifestations; moreover, her weight increased by 7 kg. (15 lb. 7 oz.). During this period massage was continued until total recovery. The last examination (April, 1949) showed that she had completely recovered.

Summary

A case of subacute thalliotoxicosis caused by swallowing 45 g. of a rat-killer paste containing 2% thallium sulphate is described. A total of 2.85 g. of BAL was given in the course of 13 days. The patient fully recovered.

The pharmacology of the drug is described, together with the reasons for using it in poisoning by thallium.

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The need for new legislation for the prevention of smoke was the principal theme discussed on September 29 at the conference of the National Smoke Abatement Society in Harrogate. Reports of the limited success and difficulties of several local authorities in administering new local Acts of Parliament emphasized the form that new laws must take if they are to be effective in preventing, rather than just abating, smoke. Strong criticism of the opposition of "big industry" to a new Parliamentary Act obtained by the city of Birmingham, which had led to a serious weakening of its smoke clauses, was made by Dr. W. R. Martine, Senior Assistant Medical Officer of Health. In contrast, an officer of the Smoke Control District of Los Angeles, who was present as a visitor to the conference, described the effective and far more stringent regulations imposed in California and many American cities. Dr. Metcalfe Brown, hon. secretary of the Manchester and District Regional Smoke Abatement Committee, reported on an investigation in the Carrington area, near Manchester, where one of the country's biggest power stations is being erected, and other industries are causing concern. Local authorities around the area are co-operating in running a network of instruments, extending over 36 square miles, to measure the pollution of the air for comparison with conditions when the power station is operating. In conjunction with this a survey on the effects of smoke and fumes on plant life—an important matter for farmers—is being conducted jointly by the Smoke Abatement Committee, the Department of Botany of Manchester University, and the Agricultural Research Council.

FATAL BRONCHOSPASMODIC CRISIS COMPLICATING MILIARY TUBERCULOSIS OF LUNGS

BY

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In a recent case of miliary tuberculosis attacks of severe dyspnoea associated with slowing of the pulse developed during streptomycin treatment. These attacks ultimately proved fatal, and as no similar occurrence appears to have been reported it seems worth while to record the symptoms and findings.

Case Report

The patient, a boy aged 11 years 9 months, had no record of serious illness and enjoyed normal health until March, 1948, when he was admitted into another hospital with a severe upper respiratory infection associated with general listlessness, anorexia, and cough. Clinical examination showed no abnormality in the chest, but radiographs revealed a shadow in the right mid-zone, which subsequently cleared. Mantoux reactions in dilutions of 1 in 10,000 and 1 in 1,000 were negative at this time. As his progress was slow he was sent to an open-air school, from which he returned at the end of July acutely ill, with a high fever and a left-sided pleural effusion. It was not until November that there was radiological evidence of miliary tuberculosis in the lungs. He was then transferred to the Victoria Hospital for Children for streptomycin therapy. No history of contact with a case of tuberculous infection was traceable in his family or companions. There was no personal or family history of asthma, hay-fever, or urticarial eruptions.

On admission (November 7, 1948) the clinical diagnosis of miliary tuberculosis with a large left-sided pleural effusion was confirmed radiologically. The Mantoux test was strongly positive with the 1 in 1,000 dilution. He had a low-grade pyrexia, and the pulse rate was 112–120 a minute. The spleen was not enlarged and no lymph glands could be felt in his neck or elsewhere. The urine showed a trace of albumin and a few casts, but no red cells. The cerebrospinal fluid remained normal throughout the illness. Despite frequent examinations tubercle bacilli were not isolated from sputum, laryngeal swab, or stomach washings.

The patient was given a three-months course of intramuscular streptomycin, with a total dosage of 77.9 g. At the end of the course, 13 days before his death, his lung condition showed both clinical and radiological improvement with resorption of the effusion. There was thickening of the left pleura and some coalescence of the miliary shadows in the right upper lobe, especially towards the hilum. No abnormality was found in the nervous system. He had a slight unproductive cough, and his weight was stationary at 57 lb. (25.65 kg.). His general condition was slightly better than on admission.

On February 12, 1949, he developed a mild coryza with some increase of the cough. Next day at noon he was seized with a bad attack of dyspnoea associated with severe apprehension and very laboured but ineffective expiration. He vomited a large quantity of mucus with some purulent-looking material, and in the course of an hour the attack gradually passed off. Scattered rhonchi and medium rales were audible over the chest, but there was no fever.

At 7 p.m. the same day a second attack occurred. On this occasion cyanosis was pronounced, and it was noticed that the pulse rate had dropped to 80 a minute. He had great difficulty in expelling air from his chest, so that expiration lasted three to four seconds—about twice as long as inspiration. This attack was relieved by a subcutaneous injection of 8 min. (0.5 ml.) of 1 in 1,000 adrenaline and by oxygen inhalation. After the attack had passed off the pulse rate was recorded at 120–142 a minute.

For 36 hours he remained free of dyspnoea and showed no abnormality except for persistent tachycardia 120–136 and a few scattered medium rhonchi on lung auscultation. On February 15 he had two more attacks, with intense expiratory dyspnoea and slowing of the pulse to 80 a minute. During both of these he lost consciousness for a few minutes.

On February 16, at 9 a.m., he had a very severe attack which lasted an hour. This time the expiratory difficulty was very great and the pulse fell to 68 a minute, though the volume was remarkably good. He became unconscious and was deeply cyanosed for 45 minutes, during which time he was given 1 min. (0.06 ml.) of 1 in 1,000 adrenaline subcutaneously at minute intervals and continuous oxygen inhalation through a glass funnel. Examination of the chest at this time, as during preceding attacks, showed no evidence of pneumothorax. The high-pitched rhonchi usually associated with bronchospasm were not heard during this attack—a remarkable finding in view of the intensity of the expiratory effort. After 45 minutes the pulse rate rose abruptly to 168 a minute and the spasm passed off, consciousness returning during the next 15 minutes. At this stage direct examination of the larynx showed no evidence of spasm of the cords. The patient was then nursed in an oxygen tent, where he regained and maintained a good colour, was quite cheerful, and ate a normal tea and supper. Examination of the chest now showed scattered rhonchi, with some medium rales in the right upper lobe. The temperature was normal and the pulse between 148 and 160, but of good volume. At 1 a.m. on February 17 he suddenly became restless, urgently dyspnoeic, and cyanosed, struggled into a sitting position, and in two to three minutes collapsed and died.

Post-mortem Findings:—Necropsy was carried out by Professor T. Crawford 13 hours after death; the following significant findings are extracted from his report.

"*Respiratory System*:—Dense pleural adhesions are present over the lateral aspect of the left lung, and the appearance suggests an organizing caseous exudate at this area. The trachea appears normal, but both bronchi are pressed upon by enlarged caseous glands surrounding them close to their origins. There is, however, no ulceration of the glands into the bronchi. An irregular caseous focus measuring 2 by 1 cm. is situated in the lower part of the upper lobe of the left lung, and around this there is an area of caseous bronchopneumonia. Three small caseous foci measuring 5 mm. in diameter are present in the right upper lobe. Small miliary lesions, just visible to the naked eye, are scattered widely through the lung tissue. The *spleen* is moderately enlarged and shows a few small tubercles in its capsule and scattered through the substance. *Lymphatic System*:—Enlarged and caseous glands are present at the hila of both lungs and beneath the bifurcation of the trachea. Further glands are present in chains extending up the sides of the trachea into the anterior triangle of the neck, and at this site both vagus nerves are firmly adherent to caseous glands. Caseous glands are also present in the portal fissure and beside the abdominal aorta. *Head*:—The brain and meninges appear normal and show no evidence of tuberculosis. *Summary*:—Primary tuberculosis of the lung; tuberculosis of mediastinal, cervical, and abdominal lymph glands with involvement of the vagus nerves; miliary tuberculosis."

Comment

Correlation of the clinical and post-mortem findings in this case suggests that the attacks of severe expiratory dyspnoea associated with slowing of the pulse and evidence of bronchospasm resulted from vagal stimulation. The vagus nerves were found adherent to caseous lymph glands, and it is suggested that the attacks were initiated by change of position affecting the adherent nerves.

Our thanks are due to Dr. Charles Pinckney for permission to publish the case and to Professor T. Crawford for his post-mortem report and for helpful advice and criticism.

Medical Memorandum

Spontaneous Disappearance of Apparently Secondary Growths in Liver

The following case contains several points of interest, particularly the finding of three apparently secondary nodules of some size in the liver during the removal of a huge adenocarcinoma of the left ovary, and the fact that they had disappeared when sought at operation two and a half years later.

Case Report

A farmer's wife aged 58 complained on September 8, 1938, of increasing size of the abdomen for six months, with some generalized pain, a dry cough, and, latterly, much dyspnoea. There had been occasional vomiting; the appetite was poor, the bowels regular. She did not think she had lost weight. For the past month she had had palpitations and swelling of the feet. There had been three normal pregnancies, and her periods had been regular until 52. Since then she had had small losses of blood at long intervals.

She was a pale, thin woman, markedly dyspnoeic; tongue clean, pulse 100/110, apex beat displaced to left, heart sounds clear, B.P. 140/90. Right chest stony dull to level of scapular spine; no adventitious sounds. Left side clear. Enormous tender regular swelling, filling abdomen, some free fluid. Small normal cervix; uterine body not felt apart from abdominal swelling. Diagnosis: a malignant cyst of ovary, unlikely to be operable.

Admitted to Royal Sussex County Hospital on September 21. Next day 31 oz. (880 ml.) of clear fluid aspirated. A radiograph showed no sign of secondary growth of lung or pleura. During the next 18 days four further aspirations averaged 38 oz. (1.08 litres). After each a radiograph was negative to growth or tuberculosis. The pleural fluid was sterile on culture. Film: polymorphs 68%, lymphocytes 30%. R.B.C., 4,100,000; Hb, 65%; C.I., 0.8; W.B.C., 11,000 (P. 77%, L. 14%, E. 2%, M. 7%). Wassermann test not done.

In view of the persistently negative *x*-ray reports for secondaries in the chest it was decided to give her an outside chance and to operate.

Operation, October 11, 1938.—Under bromethol, cyclopropane and oxygen a long paramedian incision exposed a huge left ovarian cyst, softened and necrotic in many places. A thinned-out ribbon of transverse colon was stretched across it. This and many adhesions of small intestine and omentum were separated by gauze dissection and the cyst removed: several leaks of dirty fluid and necrotic material occurred from the cyst. An apparently healthy right ovary was also removed. Three firm raised nodules, roughly 1–1½ in. (2.5–3.75 cm.) in diameter, present on the anterior surface of the right lobe of the liver, were regarded as certainly secondary growths from the malignant ovary, and for this reason, as well as the patient's poor condition, panhysterectomy of a small smooth uterus was not done.

Pathological Report.—Left ovary, a malignant papillary adenocarcinoma; right ovary, post-menopausal changes. No sign of malignancy.

The patient made a good recovery and was discharged on November 2, with a poor prognosis. During the ensuing months no further fluid collected in the right pleura and signs of pleural thickening gradually disappeared. A year later the liver was not enlarged and there was no evidence of secondaries or fluid in the abdomen. The patient felt well and had put on weight. This unexpected result was maintained throughout the second year after operation.

On March 21, 1941, however, she returned. For six months she had had small losses of blood per vaginam, with a watery discharge in the evenings, and felt tired. The abdomen and liver showed nothing abnormal: P.V., a small, firm mass, which bled on touch, protruded from the cervix and there was some thickening of the lower uterine segment. Biopsy showed the protruding mass to be adenocarcinomatous.

Second Operation.—After a few days' douching and a transfusion of 1 pint (568 ml.) of blood, operation was performed on March 25. The abdomen was opened through the old scar and the liver first examined. The only sign of the three previous nodules was a small puckered scar; the rest of the liver surface was smooth. The caecum and some coils of ileum were adherent to the uterus, and after separating these panhysterectomy was done. The lower uterine segment was much thickened and the parametrium very vascular. On detaching the former the uterine body tore away, leaving the lower uterine segment and cervix almost completely replaced by soft growth, which was already infiltrating the parametrium. There was little hope of their complete removal. It was decided to drain the canal into the vagina and to apply radium later. The abdomen was closed and 2 pints (1.4 litres) of blood given by drip. She made a satisfactory recovery and the vaginal tube was removed on the fourth day.

Two and a half weeks later radium was given—20 mg. in the cervix and a 25-mg. tube in each vaginal vault for 15 hours (1,050 mg.-hours). Another application followed three weeks later—10 mg. cervical and two 25 mg. vaginal for 15 hours (900 mg.-hours). Total for the two applications, 1,950 mg.-hours. On March 10 the patient was discharged.

In September there was a suspicion of thickening along the right utero-sacral ligament, but three months later this had disappeared and the tiny cervix was mobile. At this date the patient complained of pain in the spine at mid-dorsal level. Movements were good and a radiograph showed no sign of secondary growth. In January, 1942, this pain had gone, but another had taken its place in the lower lumbar spine. Radiographs revealed no secondary growth, but some osteo-arthritis.

In December, 1948, the patient was able to do her housework, and only the headaches and back pain bothered her. She then weighed 2 st. (12.7 kg.) more than just after her first operation.

Comment

The special point of interest is the proved disappearance, two and a half years after the removal of a malignant ovarian cyst, of three apparent secondaries in the liver. In the absence of a biopsy, however, no certain claim can be made that they were malignant. A second point is that no further growth in the peritoneal cavity ensued. Thirdly, the disappearance of all growth from the remains of the lower uterine segment and parametrium after a moderate dose of radium was hardly expected.

The three incidents together suggest not only a low grade of malignancy but an unusual degree of bodily resistance to cancer. A risk was admittedly taken in using radium with so slender a barrier between the remains of growth and the peritoneal contents.

The presence of a large pleural effusion accompanying malignant cysts does not necessarily imply metastases, as malignant growths of the ovary seldom metastasize outside the peritoneal cavity. The connexion between the occasional post-menopausal losses over six years and the malignant ovary is speculative. A certain number of such tumours do seem to provide an oestrogenic hormone which re-energizes the endometrium after the menopause. The adenocarcinoma of the uterus was almost certainly a spread from the ovary, and emphasizes the importance, whenever feasible, of doing a panhysterectomy as well as a double ovario-salpingectomy in such cases.

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Reviews

A TEXTBOOK ON TRANSFUSION

Blood Transfusion. Edited by Geoffrey Keynes, M.A., M.D., F.R.C.S. (Pp. 574; 110 illustrations. £2 12s. 6d.) Bristol: John Wright and Sons. 1949.

The great amount of work carried out upon all aspects of blood transfusion during the past decade has created many opportunities for new books. The perspective has altered completely since 1939, when Riddell wrote the last major British textbook on transfusion. For example, Riddell speculated on the possibility that incompatibility within the MN system might be the cause of minor haemolytic reactions, but there are now numerous investigators who know from their own experience that these groups are of negligible clinical importance.

This new textbook is a comprehensive guide to the whole subject. It begins with a delightful and authoritative account of the history of blood transfusion, by Mr. Geoffrey Keynes. The indications for, and complications of, transfusion are discussed at length by Dr. Bodley Scott. Mr. A. Till writes on technique, and Dr. H. F. Brewer on blood groups, the organization of a hospital transfusion service, and, with Mr. F. W. Mills, on the blood donor. There is a chapter about transfusion in infancy by Professor R. W. B. Ellis, an account of blood storage by Sir Lionel Whitby, and a particularly lucid and thorough chapter on blood derivatives and substitutes by Dr. R. I. N. Greaves.

It is natural that in a book of this size and scope, written by a number of different authors, there should be signs of unevenness. For example, almost a page is devoted to a description of the rare antigen C^w, which is of very small importance in blood transfusion. By contrast, a reader wanting to know how old a bottle of stored blood can profitably be given to an anaemic patient must be content with brief, conflicting dicta appearing in different sections of the book. On page 84 he is told that "for the relief of chronic anaemia . . . stored blood should not be used"; but he must somehow try to reconcile this with the statement on page 459 that "blood . . . stored for a period of 14 to 21 days is almost as good as fresh blood for the treatment of simple anaemia." If the reader were given some quantitative data on the survival of erythrocytes stored for different periods in acid citrate-glucose solutions he could judge for himself which of these two statements is the more reasonable. A certain number of fallacies, derived from other authors, have found their way into the book. For example, it is said in connexion with transfusions to infants with haemolytic disease that if the red cell count is raised above a certain level (3.5 million/c.mm.), the excess red cells will be lysed. This concept is unquestionably incorrect. A second example is a formula given for calculating the amount of blood to transfuse to an infant. This assumes a blood volume of 110 ml./kg., but, except in plethoric infants, who are unlikely candidates for transfusion, the blood volume is in fact approximately 75 ml./kg.

These and other occasional lapses make one hesitate to describe the whole book as authoritative, though there is no doubt that large sections of it deserve that title. In any case its wide scope and discriminating lists of references will ensure its value to all who practise blood transfusion.

P. L. Mollison.

INVESTIGATION OF THE RENAL TRACT

Cystoscopy and Urography. By Jas. B. Macalpine, F.R.C.S. Third edition. (Pp. 570; 338 illustrations and 15 coloured plates. £3 3s.) Bristol: John Wright and Sons. 1949.

The second edition of this well-known work was a war casualty. All the copies of that edition and the materials for a reprint were destroyed by bombs, so that the book was unobtainable for many years. The only benefit that accrued from the misfortune was the time afforded the author to bring it up to date.

The chapter on urinary tuberculosis has been largely rewritten and a new section on its pathology has been added. Cystoscopy is only one of the steps in the routine investigation of a urological case, and the findings must be correlated with other methods of obtaining information. The author has therefore done well in not confining his attention to cystoscopy and posterior urethroscopy. This allows consideration of other questions—whether, for instance, the rapid secretion of radio-opaque dye and a dense shadow of an apparently normal pelvis is sufficient guarantee that the kidney on that side is free from tuberculous infection. It is well known that there are two schools of thought on this subject, some urologists insisting on catheterization of the ureters and others relying on the cystoscopic and pyeloscopic findings. Mr. Macalpine favours an intermediate course. He "accepts the urographic evidence of disease in the principally affected kidney and gives due weight to the pyelogram of the other side." He recommends that cystoscopy be limited to a quick inspection of the bladder and an indigo carmine test, the danger of producing a secondary infection being thereby reduced. The least satisfactory paragraphs are those describing the endoscopic resection of the prostate. Here the author relies more on the writing of others than on his own experience and there is a loss of that personal touch which characterizes the rest of the book. A new section on the punch-operation for prostatic hypertrophy by means of the technique used at the Mayo Clinic has been contributed by Mr. R. H. O. B. Robinson.

This book established itself as the best English work on this subject long ago, and the new edition should more than maintain its previous reputation. It is clearly written, practical in its outlook, and the illustrations and coloured plates are excellent.

Kenneth Walker.

CHEMISTRY OF ALKALOIDS

The Plant Alkaloids. By Thomas Anderson Henry, D.Sc.(Lond.). Fourth edition. (Pp. 804. £3 3s.) London: J. and A. Churchill. 1949.

Everyone interested in plant alkaloids, whether botanist, chemist, or pharmacologist, owes a great debt of gratitude to Dr. Henry for the way in which, at intervals of about ten years, he has brought his book up to date. At its first appearance in 1913 it was a substantial volume of some 480 pages. Each successive edition incorporated much new material, and the present contains something like three to four times the number of words as the original volume. Apart from a description of the purine alkaloids which was omitted from the second edition, the introduction of new material has not involved jettisoning the old, and the present book is probably the most authoritative and exhaustive work on the plant alkaloids that has ever been written.

Those who have used this book for many years—and there must be many who have the first, second, and third editions on their shelves—will be pleased to find in the new volume all the valued features of its predecessors. The botanical origin of groups of alkaloids is discussed as carefully as ever and has been brought up to date. The sections giving an account of the pharmacology of the alkaloids are admirable, some of them have been considerably enlarged, and the synthetic substitutes for natural alkaloids have been briefly but adequately described. Indeed, these sections provide as good an introduction to the relevant literature as can be found.

The main bulk of the book is concerned with the chemistry of the alkaloids, in particular with the difficult structural problems presented by these fascinating natural products. Dr. Henry is here a master of his subject. Full justice is done to all relevant research, but the reader is never weighed down by the immense mass of experimental evidence, because the author guides him skilfully through intricate argument and counter-argument and illuminates his path with innumerable structural formulae. The narrative is made vivid by the inclusion of small practical details, such as the experimental conditions of many reactions and the physical constants, crystalline appearance, and solubilities of innumerable substances. It is probably this feature which has made earlier editions so

popular among alkaloid chemists. Dr. Henry has always kept close to experimental details, so that in this comprehensive work he has found space to remark that strychninolone crystallizes in "glistening prisms" and berberal in "colourless glancing leaflets." He has the delight of the craftsman in his subject; just as the carpenter caresses a fine piece of wood with his hands, so Dr. Henry's pen cannot resist a tribute to a beautifully crystalline substance.

A final word must be given about the reference lists which are distributed throughout the work. In many years' use of earlier editions I have never found a reference inaccurately quoted, and study of one or two lists in the present edition has shown no important reference to be omitted.

H. R. Ing.

MONOGRAPH ON RHEUMATISM

Manuel Pratique de Rhumatologie. By Professor Gunnar Kahlmeter. (Pp. 134; illustrated. No price). Paris: Expansion Scientifique Française (23, Rue du Cherche-Midi).

Many English readers will welcome this French translation of Kahlmeter's manual of the rheumatic diseases. They will find a simple and unpretentious little book, written with a brilliant power of clinical exposition and lucid argument. There are no references, for this is Kahlmeter's thought and experience; there is no index, for this is a book to read, not a work of reference.

The important chapters are those on acute rheumatism and rheumatoid arthritis. The author regards them as closely related conditions, and argues the matter so well as to be almost convincing. Discussing the aetiology of rheumatoid arthritis, he inclines to the hypothesis of "allergy," but by this he means a specific mode of reaction to a number of causal agents. "Lorsque, dans la théorie allergique moderne," he writes, "on fait usage du mot *allergie*, ce mot doit être pris, non dans sons sens original, mais plutôt dans celui de 'mode spécifique de réaction.'" This simply will not do. It is as if a chemist should write, "Sodium chloride is to be taken as meaning anything with a salty taste." Allergy has a precise meaning, which is not "a specific mode of reaction," and it is not open to Professor Kahlmeter or anyone else to tamper with the meaning of scientific terminology.

There are concise descriptions of "infective pseudo-rheumatism" (the nomenclature throughout is that most familiar to French readers); of osteoarthritis; of spondylitis; of rheumatism of the menopause; of tendinitis and bursitis; and a less satisfactory chapter on myalgia.

The author's experience in therapeutics is of particular interest. It is refreshing to find due attention given to medicinal measures, for we in this country rely far too much on physiotherapy, but it is surprising to read that the author has found colchicine of value in rheumatoid arthritis and in rheumatism of the menopause. After reading his warm advocacy of *x*-ray therapy in rheumatoid arthritis, bursitis of the shoulder, and tendinitis, especially that associated with osteoarthritis of the hip and knee, English readers may feel that a more extended trial of the method should be made in this country.

Kenneth Stone.

Dr. Lowrain E. McCrea's *Clinical Urology* (second edition; pp 503; 263 illustrations, 7 in colour; $6.50; Philadelphia: F. A. Davis Company, 1948) is an excellent book, and the first edition, which appeared in 1946, met with great success. It is written for practitioners, and its object is to tell them what the diagnosis is likely to be, how the patient should be treated, and the best means of carrying out this treatment. Not a word is wasted, and when words can be reduced in number by the use of an illustration the illustration is provided. The plates and diagrams are of high standard, and merely by looking at them a tired general practitioner at the end of a long day's work could obtain a good knowledge of urology. A book which lays down rather than discusses methods of treatment must necessarily be dogmatic, but dogmatism here is not obtrusive; the author only states that the methods he prescribes are those that have given the best results in his own experience. It is perhaps necessary to add that the paper, the printing, and the general production are such as one would expect from a country where publishers have not been handicapped by the austerities produced by the war.

BOOKS RECEIVED

[Review is not precluded by notice here of books recently received]

Varicose Veins. By R. Rowden Foote, M.R.C.S., L.R.C.P., D.Obst. R.C.O.G. (Pp. 226. 32s. 6d.) London: Butterworth. 1949.

Modern Practice in Anaesthesia. Edited by F. T. Evans, M.B., B.S., F.F.A. R.C.S., D.A. (Pp. 606. 50s.) London: Butterworth. 1949.

Collected Papers of the Mayo Clinic and the Mayo Foundation. Edited by R. M. Hewitt, B.A., M.A., M.D., and others. Vol. 40. (Pp. 918. 55s.) Philadelphia and London: Saunders 1949.

Masochism in Modern Man. By T. Reik. (Pp. 439. 25s.) New York: Farrar, Strauss. London: George Allen and Unwin. 1949.

Understand Your Diabetes. By J. W. Caldwell, M.D. (Pp. 145. 7s. 6d.) Toronto: Oxford University Press. London: Geoffrey Cumberlege. 1949.

Les Lipides. (Pp. 399. 1,000 francs.) Paris: Éditions du Centre National de la Recherche Scientifique. 1949.

Les Méthodes Statistiques dans l'Expérimentation Biologique. By P. L'Héritier. (Pp. 93. 400 francs.) Paris: Centre National de la Recherche Scientifique. 1949.

Unites Biologiques Douées de Continuite Genétique. (Pp. 205. 1,000 francs.) Paris: Centre National de la Recherche Scientifique. 1949.

Le Trincee Cliniche della Tonsillectomia. By G. Calderoli. (Pp. 78. No price.) Bergamo: Carrara. 1948

Sexual Freedom. By R. Guyon. (Pp. 344. 16s.) London: John Lane, The Bodley Head. 1949.

Neurology. By R. R. Grinker, M.D., and P. C. Bucy, M.D. 4th ed. (Pp. 1,138. 63s.) Oxford: Blackwell Scientific Publications. 1949.

Aids to Forensic Medicine and Toxicology. By W. G. Aitchison Robertson, M.D., F.R.C.P.Ed. Edited by J. H. Ryffel, B.Sc., F.R.I.C. 12th ed. (Pp. 170 4s. 6d.) London: Baillière, Tindall and Cox. 1949.

Leptospirosis. By A. A. Ayala. (Pp. 201. No price.) Barcelona: Ediciones Byp. 1949.

Notes on the Theory of Dental Surgery. By N. Black, L.D.S. R.C.S. (Pp. 168. 12s. 6d.) London and New York: Staples Press. 1949.

Fractures and Dislocations in General Practice. By J. Hosford, M.S.Lond., F.R.C.S. 2nd ed. revised by W. D. Coltart, M.B., B.S.Lond., F.R.C.S. (Pp. 290. 21s.) London: H. K. Lewis 1949.

Discoverers for Medicine. By W. H. Woglom, M.D (Pp. 229. 18s.) Yale: University Press. London: Cumberlege. 1949.

Orthopädische Gymnastik. By G. Hohmann and L. Jegal-Stumpf. 2nd ed. (Pp. 124 M. 8.70.) Stuttgart: Georg Thieme. 1949.

Pharmaceutical Emulsions and Emulsifying Agents. By L. M. Spalton, B.Pharm.Lond., M.P.S. (Pp. 132. 5s.) London: The Chemist and Druggist. 1949.

Handbook for the Identification of British Insects. Diptera. Vol. 9. Part I. By H. Oldroyd. (Pp. 49. 7s. 6d.) London: Royal Entomological Society of London. 1949.

Die Chirurgische Abteilung des Burgerspitals Basel zur Zeit der Antiseptik. By G. Reichen. (Pp. 107. No price.) Aarau: Sauerländer. 1949.

The Trend of Scottish Intelligence. Sponsored by the Population Investigation Committee and the Scottish Council for Research in Education. (Pp. 151. 7s. 6d.) London: University of London Press. 1949.

A CHOLERA CENTENARY

BY

MAJOR GREENWOOD, D.Sc., F.R.C.P., F.R.S.

More than 270 years ago Sydenham predicted that the epidemic diseases which he saw would give place to others the nature of which it was impossible to foresee. He was writing some ten years after the last epidemic of plague on a grand scale in Great Britain. Just a hundred years ago our great-grandfathers, to whom plague was a distant memory, suffered the second epidemic of Asiatic cholera, which has not afflicted us since 1866. In London the worst week was that ending September 8, 1849, with 2,021 deaths; four weeks later the total had sunk to 288, and the epidemic rapidly declined. It killed more than 50,000 persons in England and Wales—about as many as the war in the air of our time. Now we study with a certain anxiety the much smaller figures of notified poliomyelitis; with a certain anxiety because, epidemiologically speaking, we do not know so *very* much more about it than our great-grandparents knew about cholera. Sydenham was a good prophet. The cholera of 1849 was the subject of three bulky reports, by the General Board of Health, by the College of Physicians, and by the General Register Office. Copies of them, even those in an epidemiological department, need to be handled cautiously in these days of soap-rationing; they are apt to be very dusty. That published by the College of Physicians is the most readable because it is not very statistical and is the work of a single author, William Baly (1814–61), a physician of sufficient importance to be remembered by D.N.B., but hardly even a name to most of us.

William Baly, a student at University College and Bart's, graduated M.D. at Berlin in 1836, became physician to the Millbank Penitentiary in 1841, and F.R.C.P. in 1846; he was thought to be a rising man, and was appointed physician to the Queen, as understudy to Sir James Clark, in 1859. He was killed in a railway accident when 47. His report is quite readable and strictly orthodox, as the official report of a professional body is sure to be. A reader in 1949 may say that, generally speaking, when Baly was quite sure, he was quite wrong, and when he doubted he inclined to the wrong side. That, however, is a grossly unjust way of judging an official report made by a young man a hundred years ago. We are children of our age, deserve blame if, intellectually and morally, we are behind it, but certainly none if we fail to anticipate future discoveries.

In 1849 Galenical epidemiology was well stricken in years but still vigorous; Southwood Smith (1788–1861) and John Sutherland (1808–91), two of our best practical epidemiologists, were Galenists in the sense that the epidemiological importance of tainted air, of miasma, was to them much greater than that of contagion. There was indeed then living one man, Jakob Henle (1809–85) who published in 1840 in his pathological researches a remarkable essay on miasmas and contagions (it was reprinted, in Sudhoff's series of Klassiker der Medizin, in 1910) which Baly might have read. Henle's argument was, briefly, this: that while in ancient medicine most epidemic diseases were reckoned to be miasmatic, now—viz., in 1840—only one, malaria, would be universally regarded as purely miasmatic; three—syphilis, scabies, and hydrophobia—would be classed as purely contagious. All the others—smallpox, measles, cholera, etc.—he classified as miasmatic-contagious, but very plainly indicated his opinion that the emphasis should be on the contagious side. He then—as had Fracastorius (1483–1553) nearly 300 years before—put forward the idea of a living contagion, perhaps a minute vegetable organism, as the specific biological cause of each disease and, more fortunate than Fracastorius, could point to a striking analogy, the epidemic disease of silkworms—muscardine—which had been proved by Bassi and Audouin, a few years before he wrote, to be due to a vegetable parasite. But Henle could not *demonstrate* any such *contagium vivum* in connexion with human epidemic diseases, excluding scabies.

Baly does not mention Henle, but he does speak of John Snow (1813–58), who had already urged that cholera was a water-borne disease, and, quite courteously but emphatically, rejected his conclusion. Probably if Baly had written four or five years later he would have taken Snow much more seriously, because Snow's conclusive statistical proof that, as we should now say, mortality from cholera and the drinking of polluted water were highly correlated was based upon the epidemic of 1854. Baly, although no statistician himself, had a considerable respect for statisticians and whole-heartedly accepted Farr's demonstration that low altitude and high mortality from cholera were highly correlated. Indeed, it was the basis of his general argument, which was this. The cholera poison is not a vapour or miasma but a solid "something" usually conveyed by air currents. If this "something" reaches a low-lying district, harbouring a poverty-stricken, overcrowded population where filth accumulates, then cholera will arise; low-lying, damp, foggy sites were sites of election. He contrasts the erratic lines of travel and the persistence of cholera with the universality of the great influenza of 1847–8, which no doubt he considered a typical purely miasmatic disease. He was fair-minded; he admitted the possibility—indeed, the probability—that the cholera poison might be introduced by other means, that the disease *might* be contagious. He is, however, almost as reluctant to accept contagion as a *vera causa* as was Henle to admit miasma as a reality.

What must strike a modern reader, and might have struck a contemporary, as Baly's weakest dialectic is in his discussion of how the Asiatic cholera reached Europe and America. He agrees that the cholera could spread against the wind, in the teeth of the Monsoon; he agrees that it followed the line of human intercourse, that it entered at the ports, moved up waterways, and so on. Surely it was easier to suppose that the continuance of cholera in a ship was due to the persistence and multiplication of a *contagium vivum* in the bodies of the patients than to try to exclude contagion from one's argument? That once admitted, conversion to Henle's standpoint would follow. But it is easy to be superior; we know much more about cholera than even Henle and Snow, but no epidemiologist would be bold enough to explain why the epidemic of 1866 was our last.

Baly's section on preventive measures is very short and is no more than a colourless abbreviation of what Southwood Smith and Edwin Chadwick had recommended much more forcibly for the mitigation of *all* epidemic diseases. The devil's advocate may ask whether if the College of Physicians in 1849 *had* officially endorsed what we now accept as the right theory, Snow's theory, many lives would have been saved. I think the answer must be "No."

There is a sentence in Baly's report which was only too true.

> "Quarantine can no longer be adopted as the means of preventing the entrance of Cholera into England; for it is incompatible with the present state of commercial intercourse, and with the well-being of a commercial country."

Perhaps quarantine would not have kept cholera out, but time was to show that something more than fear of epidemics was needed to persuade the electorate to clean up the country.

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FAT ABSORPTION

The absorption of the amino-acids and the monosaccharides which are released by the digestion of proteins and carbohydrates in the small intestine is a comparatively simple process, or at least it is generally described as though it were a simple process. But there can be no illusions about the extreme complexity of the processes which are involved in the absorption of fats. In last week's *Journal* (p. 719) we published an authoritative review by Professor H. S. Raper of the experimental evidence which has slowly accumulated during the last 50 years, and the changing interpretations that have been applied to the available information. The "classical theory" which was accepted a generation ago can be briefly summarized. It stated that the food fats undergo complete digestion in the small intestine to glycerol and fatty acids; the latter cannot be absorbed as such because, being insoluble in water, they cannot pass through animal membranes. The fatty acids are converted by the alkalis of the digestive juices in the intestine into water-soluble soaps and absorbed in this form. As neither fatty acids nor soaps are found in the thoracic duct, it was presumed that the absorbed soaps are reconverted in the epithelial cells of the intestine into neutral fat and as such are transported into the lacteals.

This familiar story needed serious amendment when it was demonstrated that the reaction of the intestinal contents was generally too acid to permit of soap formation and that, furthermore, there is not enough base available in the digestive juices to convert all the released fatty acid into soap. The question that needed an answer was how the insoluble and indiffusible fatty acids were converted into the soluble and diffusible form necessary for their passage through the intestinal membranes. Verzar and his colleagues have shown that the bile acids can either combine chemically with the fatty acids or else become associated with them in some looser form as a so-called "complex." The resulting product is soluble and diffusible. This solvent or "hydrotropic" action of the bile acids is enhanced by the lecithin of the bile. Verzar's theory had to meet the objection that there is insufficient bile acid available in the intestine to dissolve all the released fatty acid; but he went on to suggest that after the bile-acid–fatty-acid "complex" enters the intestinal epithelium the bile acid is split off, returns to the intestinal lumen there to pick up a fresh load of fatty acid, and continues to travel back and forth until all the fatty acid is absorbed. The freed fatty acid in the epithelial cells was thought by Verzar to pass through an intermediate phosphatide stage before being re-formed into neutral fat. Phosphatide formation involves the temporary uptake of inorganic phosphate and may be catalysed by the enzyme phosphatase which is present in high concentration in the intestinal mucosa. Some of the evidence supporting the phosphatide hypothesis may be noted: the addition of phosphate or of glycerophosphate to the intestinal contents increases the rate of absorption of fatty acids from a mixture of fatty acids, bile acids, and glycerol; iodoacetic acid and phloridzin, which inhibit phosphatase, depress fatty-acid absorption, and the use of staining methods of doubtful validity purports to show that when these poisons are used fatty acid absorption is blocked because phosphorylation does not occur. It is disappointing to learn that recent studies with radioactive phosphorus have not helped to clarify this problem.

During the last few years Professor A. C. Frazer and his colleagues, of the Birmingham school, have studied the whole question of fat absorption, and the paper on fat metabolism and the sprue syndrome which Professor Frazer read at the Annual Meeting of the B.M.A. in Harrogate last June is published in the opening pages of this issue. The novel features of the hypothesis of the Birmingham school are, first, that fat digestion in the intestine is normally very incomplete; secondly, that neutral fat is absorbed as such in the form of minute emulsified particles; and, thirdly, that the soluble fatty-acid–bile-acid complexes pass directly from the intestine into the portal blood and do not travel via the lacteals. Frazer refers to his theory as the "partition hypothesis," because it supposes that there are two routes for fat absorption—via the lacteals or directly into the blood. Fat particles, so-called chylomicrons, can be detected in the blood under dark-ground illumination as points of light and counted; during starvation they are scanty, but after a fat meal they increase in number. If rats are given well-emulsified olive oil the lacteals appear milky, and the chylomicron count in the systemic blood rises but that in the portal blood remains low. It is concluded that the absorption of neutral fat occurs via the lacteals into the systemic circulation. On the other hand, if a mixture of fatty acids and glycerol is administered the lacteals remain relatively free from fat, but the chylomicron count in the portal blood rises sharply; the fatty acid, on reaching the liver, is retained there and the systemic chylomicron count remains low. It is worth recalling in this connexion the work of Munk, who found, 60 years ago, that only about two-thirds of the absorbed fat can be recovered by "cannulating"

the lymphatics, and concluded that the missing third is absorbed by some other route, possibly directly into the blood stream. If cetyl sulphate is added to neutral fat introduced into the intestine it has two main effects: it produces a very fine emulsion and it inhibits the action of lipase. Though in these circumstances the neutral fat cannot be hydrolysed to fatty acid, it was found by the Birmingham school that fat is absorbed quite rapidly: the lacteals soon become milky, and fat quickly appears in the systemic blood, whence it is deposited in the fat depots but not in the liver.

As Professor Frazer sees it, the most important prerequisite for the direct absorption of neutral fat is its thorough emulsification into particles which are less than 0.5 μ in diameter. The suggested mechanism of emulsification is as follows. Lipase acts on the neutral fat—i.e., the triglyceride (glycerol + three molecules of fatty acid)—in stages, splitting off successively each of the three attached fatty-acid molecules. Removal of one fatty-acid molecule leaves a diglyceride (containing two molecules of fatty acid); removal of the second fatty-acid molecule leaves a monoglyceride (containing one molecule of fatty acid); removal of the third fatty-acid molecule leaves glycerol. Frazer claims that in normal conditions fat digestion is incomplete and that lipolysis comes to a standstill before 30% of the fatty acid contained in the triglyceride is released. The end-products of fat digestion would then be (to use an Irishism) mainly undigested neutral fat together with partially split products (diglyceride and monoglyceride), fatty acids (derived from incompletely and completely split triglyceride), and glycerol. An emulsion of neutral fat of the necessary fine particle size which is stable at the *p*H and in the other conditions found in the intestine can be prepared *in vitro* by mixing neutral fat together with its partially split products (diglyceride and monoglyceride) and the soluble bile-acid–fatty-acid "complexes." This mixture of ingredients is of course exactly the one which is supposed to be present in the small intestine as a result of the preliminary partial digestion undergone by neutral fat in the presence of bile. The newer views reinforce the classical opinion that in normal circumstances both lipase and bile are indispensable for efficient fat absorption, though the way in which these substances act is now described in different terms. Frazer seems willing to accept in a general way Verzar's view that the passage of the emulsified neutral fat particles through the intestinal epithelium may involve transient phosphatide formation. It is likely also that absorption is influenced by local concentrations of electrolytes, by hormones, and even by vitamins. There is a possibility that the adrenal cortex, by regulating electrolyte balance in the body fluids, may be a subsidiary regulating factor. It is now well established that very finely emulsified liquid paraffin in which the particle size is less than 0.5 μ can be absorbed to the extent of 40% by the rat intestine. Fortunately medicinal liquid paraffin, when used in cooking or as a laxative, is not sufficiently finely dispersed to be absorbed to a significant degree in man.

How does all this fresh work aid understanding of the various clinical conditions associated with steatorrhoea? The new theories agree with the old that in the absence of bile or lipase excessive amounts of fat will be lost in the faeces. But the more obscure kinds of steatorrhoea still remain unaccounted for in spite of much careful work, which is well reviewed by Professor Frazer in his paper. In normal individuals over 95% of the ingested fat is absorbed; in the sprue syndrome the percentage falls to 50–80. It is generally agreed that in sprue the percentage of the ingested fat which is absorbed is not dependent on the total amount of fat in the diet. Thus the percentage of fat ingested remains on an average about 60 whether the total fat eaten is 65 or 95 g. daily. The impaired absorption of fat is not due to deficiency of lipase or of bile, nor is it due to inadequately fine emulsification of fat in the intestine. There is then some undetermined fault in the mucosa which hinders the transfer of particulate neutral fat into the lacteals. In other words, it is among the incompletely revealed processes which are concerned with fat absorption that the cause of sprue and related conditions must be sought. The failure in sprue is not limited to absorption of fat; it affects glucose absorption also. Study of Frazer's paper will doubtless suggest many new lines of inquiry.

PROGRESS IN OBSTETRICS

In similar papers read on both sides of the Atlantic last year Haultain[1,2] outlined the progress made in obstetrics over the past twenty years and suggested further possible improvements. His review, which is based on hospital statistics, records a progressive fall in maternal mortality and morbidity which is gratifying to read. Equally noteworthy is the improvement in recent years in the hospital figures for stillbirths and neonatal deaths. Changes for the better in social, economic, and nutritional conditions, the employment of suitably qualified resident obstetricians, advances in medical knowledge and technique, the applications of chemotherapy, and the wide use of blood banks—all played a part in increasing the safety of mother and baby. Haultain rightly emphasizes that in so far as the baby is concerned some of the credit must also be given

[1] *Edinb. med. J.*, 1948, **55**, 463.
[2] *Amer. J. Obstet. Gynec.*, 1948, **55**, 733.
[3] Ibid., 1946, **51**, 492.
[4] *British Medical Journal*, 1949, **1**, 260.
[5] Ibid., 1945, **2**, 294.
[6] Ibid., 1935, **2**, 1143.

to the advent of the paediatrician on to the staff of the maternity hospital. But progress has not been confined to institutional midwifery: the provisional figures for 1948 for the whole country are very impressive, with the maternal mortality rate 1.02 per thousand births, the stillbirth rate 23.1 per thousand births, and the neonatal death rate 19.7 per thousand live births.

At first sight these figures appear to eclipse those which are recorded in recent annual reports from the larger and teaching maternity hospitals, the efficiency of which is usually measured by their vital statistics. The discrepancy, however, is accounted for first by the fact that the Registrar-General's figures for maternal mortality, unlike those from the hospitals, exclude deaths from associated diseases—heart disease, for instance, is a common cause of death in pregnancy. Secondly, as Haultain points out, hospital statistics are greatly affected by the number of women admitted as emergencies, for, excluding those who die as a result of systemic disease, the deaths in hospital occur almost entirely among the cases in which pregnancy or labour has become complicated or has been mismanaged at home. If, however, only booked cases are considered then the hospitals can claim excellent results, even though such patients include many selected for hospital care in anticipation of an abnormal pregnancy or of a difficult confinement. It might be said here that the overall results obtained at different hospitals cannot be compared without making allowances for such factors as the percentage of cases admitted as emergencies and the social and economic complexion of the areas served by the hospitals. The general standard of domiciliary midwifery in any district can usually be appraised by analysing the numbers and types of cases admitted as emergencies to the local hospitals and the condition of those patients at the time of admission.

One method of making further progress would be to reduce the number of emergency admissions, for though in some cases they are unavoidable, in the majority they reflect either on the selection of cases for home confinement or on the conduct of the labour at home. A suggestion which was warmly received at the Twelfth British Congress of Obstetrics and Gynaecology in London last July was the establishment on the American model of a maternal mortality committee in every area to inquire into every maternal death whether at home or in hospital, and to apportion the blame constructively and instructively between patient, relatives, midwife, general practitioner, specialist, and ancillary services. In Chicago, where such a committee exists, Davis and Gready[3] concluded from the analysis of the cases at the Lying-in Hospital that two out of every three deaths could have been avoided. At the British Congress, however, some speakers were fearful that the National Health Service in its present form might hinder progress, especially so far as domiciliary obstetrics is concerned. These critics argued that the Service separates hospital from domiciliary practice, and this at a time when the great benefits resulting from the integration of antenatal, domiciliary, specialist, and hospital services, including the obstetric "flying squad," have been proved. Thus Emblin[4] was able to report that after the co-ordination of these services in his area into a municipal obstetric organization 5,000 consecutive deliveries were supervised with only one maternal death, and that due to leukaemia; at the same time the stillbirth and neonatal death rates were also reduced.

If there is still no integration of the services of those looking after the pregnant woman there is still less integration of opinions on the part obstetricians, general practitioners, and midwives should each play in making what is essentially a normal process still more safe than it is for the mother and the child. The Royal College of Obstetricians and Gynaecologists, in a report issued in 1944, considered that only general practitioners with special experience in midwifery should practise obstetrics, and it was roundly asserted in the *Practitioner* special number on the N.H.S. that "the average midwife is better trained to deal with normal midwifery than is the average general practitioner." If this is indeed the opinion of obstetricians in this country then we suggest that they should seriously look into the adequacy of the teaching they give students in hospital, and into the adequacy of the examinations conducted which enable those who pass them to have their names put on the *Medical Register*. The present attitude of obstetricians to general practitioners is but one aspect of the present tendency to see the general practitioner as someone who sorts out cases for reference to the specialist. We seem indeed to be drifting into the absurd position in which the midwife is looked upon as the specialist in normal and the obstetrician as the specialist in abnormal midwifery. A spirited defence of the general practitioner's place in domiciliary midwifery was published four years ago in this *Journal* by Dr. D. D. Logan and Dr. Eneas K. MacKenzie.[5] "Maternity practice," they wrote, "is the very root of general practice." When the writer in the *Practitioner* attacked what he called "the new type of general practitioner-obstetrician wielding the forceps" had he forgotten the pre-war type of obstetrician who wielded the knife in the practice of caesarean section? In 1935 Dr. J. Bright Banister[6] stated that the incidence of the operation was far too high, basing his observation on a series of 3,486 cases of caesarean section, 1,763 of which were taken from the reports of five large maternity hospitals in Britain during the years 1922–32. If the specialist obstetrician sees mistakes made by the general practitioner he should

recollect that the converse is also true, and the history of caesarean section between the two wars is sufficient illustration of the limitations of the expert. It is most unfortunate that these attacks have been made on the general practitioner, because they can increase neither his confidence in himself nor the confidence of his patients in him. They have created an atmosphere of competition between the general practitioner and the midwife which can lead to no good. No one appreciates the excellent work done by midwives more than does the general practitioner, but surely he can be of no use in an emergency unless he has continuous experience in the conduct of normal midwifery. It is to be regretted that the introduction of the National Health Service has given rise to these wrangles about the competence of general practitioners to do the work for which they were trained. The administrative division of responsibility has not made matters easier. What is essential is to see that the pregnant woman has the best care that can be made available, and in the provision of this the midwife, the general practitioner, and the obstetrician have their essential and complementary parts to play. The family doctor is the one person who fully understands the domestic background and psychological make-up of the woman who is to bear a child. That he should be fully competent in obstetrical technique is first and foremost the responsibility of those who teach him while he is still a student.

CAUDAL ANALGESIA

The visit of Professor R. A. Hingson to Britain this summer has stimulated interest in a new therapeutic concept, the treatment of the various conditions associated with angiospasm—such as eclampsia, reflex anuria, phlegmasia alba dolens, post-traumatic dystrophy, and gravitational ulcers—by continuous caudal analgesia. Elsewhere in this issue we publish the paper which Professor Hingson read on this subject at the Annual Meeting of the British Medical Association at Harrogate.

It had been suspected since 1934 that autonomic vasoconstrictor fibres may be inactivated by concentrations of anaesthetic which have little effect on sensory and none on motor fibres,[1] and this was confirmed in 1946 by Sarnoff and Arrowood.[2] It is thus possible, by choosing the right strength of solution, to single out for attack the vasoconstrictor impulses which are responsible for maintaining a pathologically increased tone in blood vessels. This would be of prognostic use in hypertension even if the effect lasted no longer than a single dose of procaine or amethocaine; but modern developments in the technique of epidural analgesia enable the effect to be maintained without much danger or discomfort for as long as a week or 10 days. The number of vasomotor fibres inactivated can be controlled, and it is possible by the catheter technique to abolish vasoconstrictor impulses arising from a selected band of segments. A temporary and reversible denervation of the kidney and suprarenals can thus be obtained: its completeness—and hence the degree to which the blood pressure is lowered—can be kept constant or varied from hour to hour. Hingson maintains that in certain cases of renal ischaemia the best results can be obtained by alternate dilatation and constriction of the renal vessels, on the analogy of the pavex treatment for ischaemia of a limb. This effect can be produced by alternately carrying the block above and dropping it below the level of the upper thoracic segments.

In a paper[3] published in 1947 Hingson has recorded a number of cases in which the results of treatment were impressive. As he says:

> No one can watch a hypertensive, eclamptic, comatose, convulsant patient in acute heart failure and pulmonary oedema, rescued within 30 minutes by a therapeutic continuous caudal or continuous spinal anaesthetic, which frequently lowers the blood pressure 100 mm. of mercury, and simultaneously relieves headache and blurred vision, raises the skin temperature of the feet 30° F. (16.5° C.), diminishes near fatal pulmonary oedema, slows and steadies the failing heart, increases renal output, and coincidentally abolishes pain, without appreciating that in this mechanism lies one of the most potent weapons the physician possesses to wage against disease and death.

This new therapeutic method has been described[4] as potentially the most important contribution to the treatment of eclampsia in the past decade, for it provides a means of bringing the condition under control without recourse to centrally acting depressant drugs which must increase the strain on an already strained metabolism. Control of eclampsia can usually be maintained for as long as is required, but constant vigilance is imperative.

Continuous autonomic block is not a simple method of treatment; it entails a knowledge of the physiology and the anatomy of the autonomic system and the vagaries of the caudal canal, of the pathology of the angiospastic states, of the pharmacology of local anaesthetic drugs, and a certain amount of manual dexterity. It would seem that the person best fitted to use the method is the well-trained anaesthetist, whose help in these matters is already being sought by his colleagues. However, the control of angiospastic states by this means requires individual attention for long periods, and few practising anaesthetists are able to spend enough time in the wards even to supervise to their satisfaction the post-operative care of their

[1] Heinbecker, P., *et al.*, *Arch. Neurol. Psychiat., Chicago*, 1934, **31**, 34.
[2] *Surgery*, 1946, **20**, 150.
[3] *Sth. Surg.*, 1947, **13**, 580.
[4] Dieckman, W. J., *Amer. J. Obstet. Gynec.*, 1948, **55**, 541.
[5] Apgar, V., *Curr. Res. Anesth.*, 1948, **27**, 49.

surgical patients. It may be that a number of therapeutic anaesthetists will eventually be required, familiar with such techniques as continuous epidural, segmental spinal, and lumbar peridural analgesia and with the nerve blocks appropriate to the relief of the many varieties of post-traumatic pain, and experienced in the control of the bronchoconstrictive attacks of asthma and of the vasoconstrictive attacks of eclampsia and allied conditions. To carry out this work, which is time-consuming and cannot be hurried, its practitioners would have to be freed to some extent from the obligation to spend several hours each day in the operating theatre. In the United States and Canada some steps have already been taken to overcome this difficulty, and regular nerve-block clinics, staffed by anaesthetists trained in the hard school of surgical anaesthesia, have been established at many of the larger hospitals.[5]

As a means of relieving the pain of labour and delivery continuous caudal analgesia has been very widely used in North America since its introduction by Hingson, Southworth, and Edwards in 1942, and it has been shown to be a safe and efficient method. Traditional British conservatism probably accounts for the fact that the method has not been taken up to any great extent in this country; other reasons for this may be the comparative stoicism of British mothers, the lower proportion of hospital deliveries, unwillingness to adopt the fashion for forceps which prevails in America, scarcity of anaesthetists possessing both the knowledge and the necessary time, and lack of adequate equipment, which is not yet made in this country. It should be added that other methods of obstetric analgesia are better developed in Britain than anywhere else in the world, but they nearly all entail some degree of general intoxication and transplacental narcosis, and they are thus unsuitable for the handicapped mother or for the premature infant. There is no doubt that continuous caudal analgesia can confer benefits to mother and baby which they should not be denied, and it is to be hoped that obstetricians in this country will not be satisfied until they can obtain it at least for those mothers for whom it is specially indicated.

RADIATION INJURY

The development of atomic energy research has led to a great increase in the number of people exposed to ionizing radiation. Before this development took place the number exposed to risk was comparatively small; many had some knowledge of the biological effects of radiation and nearly all had an appreciation of the possible dangers and necessary precautions. Conditions of work and the measures to be taken for protection were laid down by the British *X*-ray and Radium Protection Committee, an unofficial body formed in 1921, whose recommendations were widely accepted. Methods of handling radioactive materials and of using *x*-ray apparatus became as much matters of care and routine in most radiological departments as are aseptic surgical techniques in operating theatres. Occasional cases of injury have occurred from time to time, however, usually as the result of lack of care or inadequate knowledge. Hultberg[1] has recently published an account of two such cases—one in a surgeon who suffered acute and serious injuries to his hands and in whose blood also some changes were noted after the use on seven occasions of fluoroscopy to control the reduction of fractures; the other in an industrial worker engaged for two years in the fluoroscopical examination of castings, who paid for his disregard of the regulations by the loss of both index fingers.

Work on atomic energy has progressed in secret, and the damage done to human lives in the U.S.A. and Russia during the preparation and testing of atomic bombs is not known. From the information available it appears that serious accidents have been few considering the urgency and vast extent of the efforts made and the large number of work-people who had no understanding of the danger that they could neither see nor feel. Reports of damage have appeared from time to time; the latest, published last month,[2] gives an account of four men injured during tests at Enewetok Atoll, the United States Atomic Energy Commission's proving grounds. Fortunately the men received only a small dose of total body irradiation with gamma rays, but the beta ray doses to their hands were high and the damage serious and permanent. Exposures varied from 40 to 60 minutes. The man least affected had a severe erythema and vesiculation, but the lesions healed with only a little residual reddening at the end of a year. The other three had skin, and in one case tendon, necrosis; prolonged treatment with grafting was required and at the end of a year much disability still remained with the prospect of possible late effects still to come. The details of the tests are secret, but the general account of how this accident occurred is most significant: "This work involved the handling of radioactive materials which emitted large amounts of beta and gamma radiation. A deviation in the prescribed procedure undertaken to expedite the operation resulted in the handling of these radioactive substances directly with rubber-gloved and sometimes with bare hands rather than with the remote handling devices that had been provided." "Deviations in prescribed procedures" are generally at the bottom of such accidents, which are commonly due to lack of knowledge. Those whose duty it is to lay down regulations have to remember that they are unlikely to be carried out unless the people concerned possess some understanding of the reasons which make them necessary, and those in charge of work-people who may be exposed to radiation have to develop a sense of personal responsibility for their safety and be prepared to lose their reputation for professional competence should accidents occur.

Arrangements for protection against the dangerous effects of radiation have been admirably conducted in this

[1] *Acta radiol. Stockh.*, 1949, **32**, 17.
[2] Knowlton, N. P., *et al.*, *J. Amer. med. Ass.*, 1949, **141**, 239.

country in the past. International recommendations, based largely on the British proposals, were adopted in Stockholm in 1928 by the Second International Congress of Radiology at the instance of the British committee. Much arduous and valuable work has recently been done by the protection subcommittee of the Medical Research Council's committee on the medical and biological applications of nuclear energy and by its tolerance doses panel. Under the Radioactive Substances Act the Government has taken wide powers of control over the manufacture, supply, and disposal of radioactive substances. It has the power to impose safety regulations for occupations in which radioactive substances and irradiating apparatus are used. It is to be hoped that as more people are employed in occupations in which irradiation is a hazard tragic "deviations from the prescribed procedure" will be avoided. People with no real knowledge of the dangers do not regard official regulations in the same way as those who, understanding the dangers, accept recommendations made for their protection by their own professional bodies.

MYOIDEMA

The phenomenon of myoidema has aroused interest from time to time since it was first described by Robert Graves and William Stokes[1] in 1830. Its distinction from myotatic irritability has not always been appreciated, though most of the earlier writers were emphatic on this point. For instance, Lawson Tait,[2] who suggested the term "myoidema," insisted that a "nodule or intumescence" of muscle at the point percussed was the essential feature of the sign; he frequently observed the sulcus or linear contraction of myotatic irritability in the healthy. Although once believed to indicate pulmonary tuberculosis, and even thought to have a value in determining which side was diseased, myoidema is now usually stated to occur in most diseases associated with wasting. Denny-Brown and Pennybacker,[3] in their detailed study of fibrillation and fasciculation in voluntary muscle, observed two patients with malignant disease who presented this sign. They concluded that myoidema was a response of the whole muscle fibre to intense mechanical stimulation. It appeared to them to be an exaggeration of a normal phenomenon and unrelated to the fine fibrillation of denervated voluntary muscle or to the fasciculation so characteristic of motor neurone disease.

The cause of this increase in muscular excitability has remained a matter for hypothesis, although Koumans[4] and Seto[5] believed that malnutrition and vitamin deficiency were important factors. In this number of the *Journal* Drs. G. F. Taylor and P. W. Chhuttani bring forward further evidence supporting this suggestion. They noted the frequency of myoidema in Indian troops in the Middle East and Iraq, and in a detailed survey found that it was higher in Indians in hospital than in those on duty; higher in vegetarians than in meat-eaters; and higher in Iraq than in Syria and Lebanon, where conditions were less arduous and, perhaps, the diet better. Myoidema was less frequent in British troops than in all other groups examined. The authors were able to relate these variations in incidence with the frequency of vitamin deficiency as indicated by angular stomatitis, glossitis, cheilosis, and Bitot's spots. Severe myoidema was noted in each of 82 patients with peripheral neuritis, and its intensity diminished *pari passu* with the improvement which followed treatment with thiamin. In addition, many men with vague myalgia and muscular cramps presented intense myoidema; in these also the symptoms disappeared after the administration of thiamin. Taylor and Chhuttani conclude that in the patients they observed myoidema was related to the nutritional state and was probably a sign of thiamin deficiency. This conclusion may help to rescue myoidema from the limbo reserved for physical signs of undetermined significance and doubtful importance.

[1] *Dublin Hospital Reports*, 1830, p. 70.
[2] *On the Myoidema of Phthisis*, 1872, Dublin.
[3] *Brain*, 1938, **61**, 311.
[4] *Wien. klin. Wschr.*, 1928, **41**, 524.
[5] *J. Okayama med. Soc.*, 1937, **49**, 789.

TRICHOSTRONGYLUS AND STRONGYLOIDES

Infestation of herbivorous mammals with various species of the nematode *Trichostrongylus* is common throughout the world, far more so than human infestations, which formerly were regarded as accidental, the result of proximity to infected domestic animals. But records of *Trichostrongylus* as a human parasite have been appearing with increasing frequency, from India, Russia, Africa, N. America, and especially from the Far East, where *T. orientalis* is stated to be not uncommon as an infection in agricultural workers. The account in last week's *Journal* (p. 737), of a helminth survey in Abadan by Dr. I. S. Stewart serves to emphasize the probability that *Trichostrongylus* may have a much wider range in the human host and be more prevalent than was suspected, for in routine faecal examinations its eggs may easily be overlooked because of their close resemblance to those of hookworm. Although the degree of the infection in the Abadan survey was light, the number of positive results recorded (70%) is surprisingly high, and suggests not only that the circumstances are favourable for oral ingestion of the infective larvae but that the species appears readily adapted to the human host. The identity of this species is not yet known, but failing its determination by the recovery of adult worms at necropsy some information might be obtained by identifying the species harboured by the local sheep, which are evidently the original source of the human infection.

In quite a different category is *Strongyloides (S. stercoralis)*, a well-established human helminth which is harboured by some 35 million people in tropical and subtropical countries; its distribution is similar to that of hookworm. Unlike *Trichostrongylus*—the similar sounding name is of little significance—whose life-cycle is direct and simple, *Strongyloides* undergoes a very complex and varied development. This is exemplified particularly in its free-living or exogenous phase, which culminates in infective skin-penetrating larvae comparable with those of hookworm or in a free-living sexual generation which in turn produces infective larvae. Research in recent years has shown that the parasitic phase in the human body is also highly complex. Contrary to the belief that no

helminth can multiply inside the body of its host but must pass its offspring to the exterior, the larvae of *Strongyloides* are apparently capable of substituting an internal migration for the usual external migration. They pass from the small intestine, where the parasitic females reside, through the gut wall to the circulatory system, thence to the lungs and back to the intestine, where they reach maturity. Pulmonary changes, of which Dr. F. L. Corrigan has recently recorded an interesting example in this *Journal* (October 1, p. 738), are associated with this phase, in which, it is assumed, repeated invasion of the tissues by the migrating larvae reduces the local tissue resistance.

PROTECTING THE CONSUMER

The Government decided in November, 1943, to make the Minister of Food responsible for exercising the powers previously given by Parliament to the Minister of Health, under the Food and Drugs Act, to make regulations dealing with the composition and labelling of food. The opportunity was taken to modify statute law. The Defence (Sale of Food) Regulations altered the definition of food to include any substance used as a food for human consumption even though it is also capable of being used as a medicine, and, in addition, made it an offence to describe falsely or otherwise to mislead the public on the nutritional or dietetic value of a food. This and subsequent legislation was of such a detailed nature that the Ministry of Food undertook to advise the trade on labelling and advertising. In this way it was hoped to secure compliance with the law by the co-operation of traders. Accordingly the administration of these regulations has been based on the assumption that more can be done by persuasion to secure the elimination of misleading descriptions and claims than would be possible by the processes of the law. The achievements of the Ministry in this field of consumer protection are impressive and have brought about many changes in the descriptions of, and the claims made for, pre-packed foods and, indeed, in the outlook of manufacturers. An interesting account of four years' work in this field has recently been published.[1]

Some of the quite unjustifiable claims which came under scrutiny are quoted. A breakfast cereal food claimed "phosphates for the teeth and bones, and iron for the blood"; the label on a packet of dried herbs claimed that it provided "vitamins A, B, and C"; and there was a food consisting mainly of flour which quickly restored to health "infants in the last stages of emaciation." All of these claims and many more similar ones have been abandoned or greatly modified. There was obviously plenty of scope for reform, and the Ministry, in the exercise of a duty to the consumer about which too little is known, has based its actions and advice on certain general principles. It has been accepted that, when a name or description of a product incorporates the name of a food, that food must ordinarily be present in a significant quantity; that if the description of a food includes the names of two or more ingredients—for example, "malt extract and cod-liver oil"—the ingredient present in greatest quantity should be named first; and that qualifying adjectives which indicate the true nature of a food should be given the same emphasis as the rest of the description. On nutritional or dietetic claims difficulties have arisen not so much with the false claims for which there is no scientific foundation as with the claim which implies that a food has a dietetic or nutritional value when in fact that value is insignificant. The Ministry has taken the obviously sound view that if it is claimed that a food is nourishing it ought to contribute a significant amount of nourishment; if a food is said to be "body building" then it should provide a material amount of protein, and so on. In assessing the justification for such claims account is taken of the amount of the food ordinarily consumed in a day by the average individual. Difficulties of this kind led the Ministry to seek the advice of the Medical Research Council about vitamins and minerals in the diet, and resulted in the adoption of a code of practice which exemplifies the twin principles that nutritional claims must be justified by the presence of a significant quantity of the substance and with regard to the amount likely to be consumed by the average person.

The Food Standards Committee set up to advise the Minister has been responsible for the introduction of standards of composition for certain foods. The future programme of this committee is heavy, and many of the foods which in due course will come under review are meanwhile the subject of codes of practice. These codes, which are set out in detail in the report, represent agreement between the Ministry and informed trade opinion on the descriptions and standards appropriate for particular classes of food. They have not the force of law, but they are generally accepted by traders and have done much to protect the consumer from being misled.

[1] *The Advertising, Labelling and Composition of Food.* London, 1949. H.M.S.O. Price 1s. 6d. net.

DISTINCTION AWARDS

Consultants and specialists considered to be eligible for distinction awards are being asked by the Awards Committee to fill in a form and give details of their qualifications and experience. In this form the candidate is invited to give details of degrees and other qualifications under the heading of "university and/or medical school education," of academic distinctions such as prizes and scholarships, of clinical training and experience, of present and past appointments, and of teaching experience. He is also asked to give details of research and publications and of war service. Space is also left on the form for "any other information and remarks." In referring last week to the suggestion of a points system of assessing distinction we did not mean to imply that the Awards Committee was attempting to assess candidates without such detailed information as is now being sought.

Dr. Geoffrey Marshall, O.B.E., F.R.C.P., will deliver the Harveian Oration before the Royal College of Physicians of London (Pall Mall East, S.W.) on Tuesday, October 18, at 3 p.m. His subject is "Individuality in Medicine."

ON BECOMING A GOOD DOCTOR

BY

SIR HUGH CAIRNS, K.B.E., F.R.C.S.

We print below a slightly shortened version of the inaugural address at King's College Hospital on September 30.

Our medical world is in a state of rapid change. On the one hand we have the National Health Service, which is faced with the stupendous task of providing not only doctors and nurses but also sufficient hospital beds and good equipment to meet the needs of the nation's sick. On the other hand we have the changes wrought by medical research and discoveries in the basic sciences, and these changes have become more numerous and more important in the last 30 years than they used to be. Think only of the effect of the discovery of insulin and penicillin and of the modern treatment of anaemia. That is not all, for looming close ahead are substances which will be effective in treatment of the various types of rheumatism and cancer. You might suppose from this conjunction of changes, and from what has been said about social medicine and health centres, that the majority of the doctors of the future will spend their time in preventing disease, in keeping people well. I do not think that things will turn out that way. So far from reducing the hospital population these life-saving discoveries seem to increase the need for yet more hospital beds. Beds are required often for long periods to treat patients who would have died but for the new remedies. And more often than not these patients survive to get ill again on some future occasion. Undoubtedly there is a big field to be developed in prevention of disease and ill-health, but the fact remains that for most of us the main task of the future will be, as it has been in the past, the care of sick people. Our main objective is to become good doctors.

A Good Doctor

How does one become a good doctor? When one doctor says of another, "He is a good doctor," there is a particular meaning. You will hear the expression used not only about some general practitioners but also about some specialists. As I understand it a good doctor is one who is shrewd in diagnosis and wise in treatment; but more than that, he is a person who never spares himself in the interests of his patients; and in addition he is a man who studies the patient not only as a case but also as an individual.

Diagnosis and treatment are of course the basis of our work with patients. We learn these subjects day in and day out as we walk the hospitals, and we have to pass examinations in them. I do not propose to discuss them except to emphasize that after graduation none of us is infallible; if we accept this fact and are prepared to go on learning, our mistakes will tend to become less frequent and less serious.

How does one learn to devote oneself unsparingly to one's patients? You cannot get this from books or from formal clinical instruction. It is something which is passed on from one generation of doctors to the next, and the easiest way to acquire it is to work with a doctor who already has it in his blood. Lister, for example, was a good doctor: he used to visit his patients in King's every day, including Sundays, and his eminence and his preoccupation with research did not prevent him from showing great understanding and consideration of their feelings.

Your patients need from you more than diagnostic and therapeutic efficiency. They do not come to you to be cured; they come to be relieved of their pains and other symptoms and to be comforted. Given the choice, they would usually prefer a kind doctor to an efficient one. Never forget that the patient and his relations are usually frightened and anxious—upset in their normal life to such an extent that they are prepared to call you into their lives and to tell you the most intimate facts about themselves, though you may be unknown to them except as a member of an honourable profession. In their anxiety, especially when things are not going well for them, they may on rare occasions be rude to you and offend your dignity. This may be hard to bear, especially in the early days of one's medical life before one has lost one's self-consciousness at the bedside and has become wholly familiar with clinical technique. Under such trials you must humble yourself and continue to treat your patient with consideration and kindness, never forgetting for one moment that he is an anxious and overwrought individual, and that in seeking your advice he has paid you the compliment of admitting you to his life and confidence.

A Sense of Urgency

Emergencies teach you how to devote yourself unsparingly to your patients and give that sense of urgency which all good doctors have. To have a share in saving the life of a patient who is dying from haemorrhage, peritonitis, respiratory obstruction, or meningitis is an essential part of the doctor's education. You learn then to observe quickly, to pick out the essential points of the illness, to apply first principles of therapy promptly, and to think clearly even when you are wracked with anxiety about the patient's welfare and your own responsibility for it. This anxiety which an emergency arouses in you is an inevitable and normal reaction—enough to numb all thought but for your training. Don't run away from it, or seek to hide it beneath swagger and pomposity. Instead, familiarize yourself with it by staying with the patient at his bedside, by helping to nurse him, and by making accurate record of the events as they occur. Student nurses seem to assume their responsibilities in such cases more easily than do medical students; it is the difference between the practical and the theoretical approach to the problem of saving human life.

The good doctor, whether general practitioner or specialist, is also a man who studies the patient's personality as well as his disease. In the past this was done by the light of nature: the good doctor started by being interested in his patients as individuals, and eventually his experience taught him to size up quickly most types of mankind and to know the reaction of each type to disease. This was instinctive unformulated knowledge. But now the position has changed, thanks largely to the medical work during the recent war, when we were fighting for our lives and it was realized that the adjustment of each individual to the conditions of war, and his capacity to work and fight, depended as much upon his personality as on his physique.

The manifestations of an illness are much coloured by the personality of the patient. What you are studying at the bedside is not disease but disease in a patient. When you are asked to stitch up a cut finger it may not seem to matter very much what type of personality the patient has; though it is rather fun to try to find out without taking too much time about it. But if the patient has broken his leg, or has to undergo any prolonged illness, his subsequent successful return to his work, and his happiness at home, will largely depend on what type of man he is and the particular measures which are taken to deal with his reactions to illness. Of the people who are suddenly removed from their normal life by breaking a leg, some may be perfectly philosophical and sensible, with assured jobs to which they promptly return when the leg is mended; but others may be so constituted or circumstanced that they are consumed by genuine or imagined worries which will produce strange symptoms, symptoms which are not in the textbooks. And if not treated these symptoms will interfere with the patient's return to normal life.

The study of personality of patients is not a matter for the psychiatrists: it can be formulated on systematic commonsense lines, and it is something which all doctors can do themselves. And it can be learned by the medical student. What it amounts to in essence is that in addition to studying the patient's disease you find out about his life and work and family background. If you are prepared to give the time to listening to what he has to tell you of himself you will be richly rewarded not only by rapidly acquiring a knowledge of human nature but also by increasing your effectiveness in treatment. And the patient will have much more confidence in you than if you merely regard him as a case.

Science and Research

So far I have talked about the art of medicine, and now I must say something about the science and its relations with the other sciences. It must already be clear to you that progress in clinical medicine is largely dependent on advances in the basic and biological sciences. In my student days when we passed our examinations in physics and chemistry, and even in the pre-clinical subjects, we often said to ourselves: "Thank goodness that's over and done with." This was a short-sighted policy, and with each new application of science to medicine—such subjects as electronics, modern statistical methods, radio-active isotopes, and the application of plastics in surgery and dentistry—I find myself regretting my lack of basic scientific knowledge.

No one can hope to keep up with more than a fraction of the work which is going on, but, such is the pace and power of scientific progress, it is essential for your competence and your intellectual comfort as doctors that you should maintain a general interest in scientific matters. This sounds a tall order, but it is surprising how much you can glean from the popular scientific journals and from talking to your scientific friends. Never forget that there is so very much in medical science which is still unknown. Beyond the established knowledge that is set out in your textbooks there are many things which will be discovered in your lifetime, often with profound influence on your medical practice.

What part can the clinician himself play in research? There is scarcely a disease in which a thorough and sustained clinical investigation will not add new facts, and occasionally discoveries of outstanding importance can be made by clinicians who keep good records and are alert to observe the unusual. A recent example is the discovery by Gregg, an Australian ophthalmologist, that German measles in the early months of pregnancy may seriously damage the organs of sight or hearing of the foetus. The application of scientific discoveries in the clinical field—for example, the application of new remedies—also requires careful clinical research; and the whole clinical field is full of problems which can be worked out by a combined attack in the wards and laboratories.

Lister's Inaugural Address

One must be prepared to approach one's clinical problems on the broadest possible basis. In the last 50 years, with the growth of specialization there has been a dangerous narrowing of medical activities. I can best illustrate this trend by reminding you that when Lister was appointed as professor of surgery to this hospital his inaugural lecture was mainly on the fermentation of milk. What would people think to-day if a professor of surgery gave a lecture about milk? They would say that he was neglecting surgery and encroaching on the field of the bacteriologist or hygienist. But to Lister it was a perfectly natural thing to do. Bacteriology was a young subject to which surgeons as well as others were making important contributions. Lister owed his discovery of antiseptics to two things: first, to his thorough and persistent study, at the bedside and in the laboratory, of the healing of wounds; and, secondly, to his broad approach to the problem. When his colleague Thomas Anderson, the professor of chemistry at Glasgow, said to him one day: "By the way, have you read the papers of a French chemist Pasteur on fermentation?" Lister read these papers, and with his prepared mind at once realized that it might be the living germs described by Pasteur and not the oxygen of the air which caused wounds to putrefy. And so began his use of carbolic acid. In the lecture on milk Lister was proving again for the sceptics that there was no such thing as spontaneous generation and that the bacteria in the wound came in from the air. This principle was essential for his antiseptic system. Also in this work with the *Bacterium lactis* Lister developed a successful technique for obtaining a pure culture of a bacterium; this was the first time it had been done. Thus Lister approached his problem not only as a practising surgeon but also as a pathologist, as a bacteriologist, and as an experimenter; and, as I have advised you to do, he cultivated his scientific friends. The chemist Thomas Anderson, I have been told, not only drew Lister's attention to Pasteur's papers but also told him about carbolic acid as a possible disinfectant.

One Investigation

You may be thinking that I have been holding out to you ideals which are impossible of attainment. I have been urging you to become good doctors, to keep up with scientific progress, and to undertake research. How can one man do all these things? The answer is that no one can excel in all fields. You will evolve in different ways. Most of you should become good doctors, some will take readily to research, while others, and they will include many good doctors, will have no aptitude for it. But I do think that nearly every young doctor should try his hand at one investigation—should try to carry knowledge of some disease or symptom or function, or the effect of some form of treatment, a stage further than it has been carried before. Otherwise he will not find out what he is good for, nor will he appreciate the difficulties and labours involved in discovering new things.

I have not said anything about material objectives—careers, salaries, and so on. In medicine direct pursuit of these not unimportant aspects of life is apt to prove disappointing, and the greatest personal success is usually incidental to a life spent in service to patients or in research. That is one of the dignities of our profession. We are still, I am thankful to say, a guild, and in the course of your careers you will receive much help from your seniors which you cannot hope to repay, except by passing it on to the next generation. It remains for me only to wish you all a fruitful and happy life, and to express the hope that you will successfully maintain the fame and tradition of this great hospital.

CO-ORDINATION OF TUBERCULOSIS SCHEMES

ADDRESS BY SIR ANDREW DAVIDSON*

Sir Andrew Davidson began by saying that notwithstanding the limitations of health statistics, there was enough evidence to support the view that Scotland's health was being well maintained and, in many directions, further improved. Such a sensitive index of social health, for example, as infantile mortality was in 1948 the lowest ever recorded; and that record should be broken by the current year's figure. Yet while the prevailing trends gave reason for optimism there was no room for complacency, and there were many problems still to be solved. The most immediate one was the control of tuberculosis, which remained the black spot on Scotland's health record.

During the last war the death rate from tuberculosis rose quite steeply in Scotland; but, while in most countries the rate began to decline soon after the war was over, in Scotland it remained high, especially in the West Central area of the country and to a less extent in the Lothians and East Central area. The reason—or more likely the combination of reasons—had not been elucidated. In regard to respiratory tuberculosis, the overall Scottish position could be expressed in round numbers: there were about 30,000 names on the tuberculosis registers; 8,000 new notifications during the year 1948, when there were 3,400 deaths; some 2,500 patients awaiting admission to hospital; and nearly 5,500 beds available for treatment and isolation, of which nearly 600 were empty and unstaffed. This was the background against which schemes for controlling tuberculosis should be considered.

Development of Tuberculosis Services

Measures to control the disease did not really begin until Sir Robert Philip in 1887 established in Edinburgh the first tuberculosis dispensary in the world. Other dispensaries followed, and in 1912 pulmonary tuberculosis was made

*This address by the Chief Medical Officer of the Department of Health for Scotland was given at a refresher course on tuberculosis under the auspices of the National Association for the Prevention of Tuberculosis in Edinburgh on September 20.

notifiable in Scotland. In 1914 all forms of tuberculosis were made notifiable, and thereafter the full local authority anti-tuberculosis service gradually developed. The anti-tuberculosis service before 1948 was operated by each major local authority, the scheme being under the administrative charge of the medical officer of health. As time passed, the actual clinical work in the hospitals, and in many cases in the clinics, tended under the larger authorities to be carried out by men with special experience who might well be regarded as of consultant or specialist status. In less populous areas, however, the medical officer of health might have only a few beds at his disposal. The clinical work was carried out by himself or by an assistant, and the health visitors were too few for any of them to specialize in tuberculosis work. There was in fact every possible gradation between a highly specialized service in some of the large cities and counties and an extemporized patchwork service in some of the smaller authorities.

In the early days it was assumed, rightly or wrongly, that diagnosis and treatment, which constituted the clinical part of the work, were incidental and were possibly not quite as important as were the more preventive functions. Diagnosis, however, improved when the *x*-ray apparatus became more generally available, and special measures of treatment gradually developed also. Hence, as the years passed, the task of diagnosis tended to grow in importance; and treatment tended also to enlarge in scope.

The value of the services was best shown by the steady drop in the mortality of respiratory and non-respiratory tuberculosis. For instance, in the years 1931 to 1939 the death rate from respiratory tuberculosis fell by 12% and the death rate for non-respiratory tuberculosis by 35%. Not all of these decreases can, of course, be attributed to the anti-tuberculosis service. Improved housing, improvement of milk supplies, and the general process of social amelioration all played their part.

The purpose of the National Health Service Act in dealing with tuberculosis was not to condemn the former anti-tuberculosis service as inefficient, but rather to take the service which had showed all shades of efficiency and which had on the whole done good work and to try to improve it and strengthen it still further. The National Health Service Act unified the hospital service, and the special hospitals which dealt with tuberculosis and infectious diseases were swept into the general pool. In Scotland hospitals of all types—teaching and non-teaching alike—came within the administrative purview of the five regional hospital boards.

The environmental and preventive side of the subject was dealt with in Section 27 of the Scottish Act. The control of tuberculosis as opposed to the treatment of it remained primarily the work of the local authority. The local authority was enabled to make arrangements for the prevention of illness, for the care of persons suffering from illness, and for the aftercare of such persons, and these arrangements were subject to approval by the Secretary of State. The Secretary of State had directed that arrangements should be made by every local health authority (i.e., by the counties and by the large burghs) for the purpose of preventing tuberculosis and for the care and aftercare of persons suffering from that disease. The duties which were formerly discharged by the local authority and their medical officers of health were therefore squarely laid once more upon the same shoulders, with the exception that clinical care and hospital treatment had now been transferred to the regional hospital boards. Some of the methods by which the local authorities could discharge their obligations were as follows:

(*a*) The provision of adequate housing for tuberculous families, of garden shelters where appropriate, of night sanatoria as a means of preventing the dissemination of the disease, and the boarding out of children who were living in contact with cases.

(*b*) Provision of advice regarding segregation in the home. Provision of facilities to assist in such segregation, e.g., beds and bedding. Provision of nursing requisites, clothing, and extra nourishment.

(*c*) Provision either in co-operation with the Ministry of Labour or by the local authority themselves of suitable workshops for employment of the tuberculous.

(*d*) Provision of health visitors for services in the home and in the tuberculosis clinic.

The primary responsibility for the patient at home, and particularly for early diagnosis, must rest with the general practitioner. But the general practitioner was not working in isolation: he had all the resources of the local authority to support him, and to assist with diagnosis and treatment the regional hospital boards had been charged with the duty of providing domiciliary consultations. Regional hospital boards had the responsibility for providing dispensary and hospital services incorporating up-to-date methods of diagnosis and facilities for modern treatment. Obviously the treatment side under the regional hospital board required a double integration. It must be closely integrated with the general medical services of the area, and, perhaps even more important, with the epidemiological, social, and environmental aspects of the work. Therefore, regional hospital boards had been advised that dual appointments might be of permanent advantage in certain circumstances; that the tuberculosis officer, or chest consultant, as he was now termed, who took charge of treatment might also act under the medical officer of health in connexion with the preventive work. Whether such dual appointments were made or not, regional hospital boards must have regard to the continuing responsibility of the local authorities for epidemiological measures in their area.

Intention of the New Legislation

In the recent legislation, Sir Andrew Davidson continued, it was thought necessary to unify the hospital services under a single control in order that these services could operate generally with the maximum efficiency. The best possible use should be made of all hospital accommodation irrespective of the functions for which it was originally provided, and irrespective of the circumstances of a patient's residence. Also it was thought desirable to form a clinical tuberculosis service in which avenues of promotion would be open to those working in peripheral areas and to bring to an end many of the so-called blind-alley clinical occupations. Except in some of the larger authorities the tuberculosis officer of the past either tended to occupy one of these blind-alley positions or else accepted his post in tuberculosis merely as a step on the ladder towards an administrative post. Such a situation was not beneficial either to the tuberculosis service or for that matter to the public health service as a whole.

But no reform came without creating its own difficulties. The major difficulty which faced the tuberculosis service at the present time was ensuring full and adequate co-operation between the health officers and the hospital service. A balance still had to be kept between treatment in hospital and isolation of infection. The hospital service was to discharge both these functions. In the main the anti-tuberculosis service functioned at present much as it did in the past, although now the tuberculosis officer was the servant of the regional hospital board. In some cases he had charge of beds which he did not have before, but in all cases he must assist in carrying out the statutory preventive duties laid upon the local authorities. The net result should be that the tuberculosis officer had enhanced status. He had more fully at his disposal the resources of the hospital service for diagnosis and treatment, and he still remained the head of the tuberculosis service (under the administrative control of the M.O.H.) with the same resources as before of a clinic, clerical assistants, and health visitors.

The medical officer of health was in a position to frame new developments for his area and to ensure their application; his duties would include ascertainment. Notifications came to him, and with the tuberculosis officer he could study these notifications from the epidemiological point of view. He could ensure through his health visitor staff that the patient was suitably directed into the scheme for treatment. He could supply domiciliary aid in the way of nursing care and domestic assistance. He could give priority to the rehousing of suitable families. He could insist that his policy on examination of contacts and their further management was observed. He could enlist the service of mass radiography and ensure that it was directed advantageously towards the control of the disease. He could initiate surveys—for example, tuberculin surveys of groups of his population—adopt preventive measures, and in the near future might be able to start work with B.C.G.

It would be a mistake to attribute all the difficulties and frustration which existed at the present moment to the Health Service Act. Scarcity of hospital staff and beds, for example, were not unknown before 1948, and were probably the principal source of anxiety to all workers in the field of tuberculosis. If the old system had remained there was no reason to imagine that more hospital staff or more hospital beds would have been available. Indeed the situation in respect of hospital beds had been improved already by the new Act, and if there were no difficulty in staffing these beds a considerable addition could be made already to the number of beds available for tuberculosis. Many of the complaints about the working of the scheme would disappear if an adequate number of staffed hospital beds became available.

For achieving results in the field of tuberculosis co-operation was the definitive word and implied genuine co-operation between clinician and health officer, between hospital service and local authority, between hospital service and general practitioner, and between local authority and general practitioner. It meant an active partnership where each member of the team saw not only his own facet but something of the whole picture. Some might be tempted to have a certain cynical regard for the word "co-operation"; but the administrative structure had been laid down and must be assumed to have some permanence, and the various services, hospitals, local authorities, and general practitioners must work together. In all this, the health officer and the health visitor had a major part to play.

LOCAL HEALTH AUTHORITIES AND TUBERCULOSIS

PREVENTION AND CONTROL

A joint meeting of the Society of Medical Officers of Health and of the National Association for the Prevention of Tuberculosis held in the Great Hall of B.M.A. House on September 15 was attended by some 130 delegates.

Professor R. H. Parry, president of the society, was in the chair and was supported by Sir Robert Young. He said this joint meeting gave them an opportunity to exchange views on the arrangements made by local health authorities for prevention, care, and aftercare under Section 28 of the National Health Service Act, 1946. He said that they were now just beginning to find their feet, and it was an appropriate time for reviewing the position in regard to the biggest public health problem of the day.

Sir Allen Daley said that real prevention of tuberculosis was founded on conditions of life—housing, general nutrition, and hygiene. Some years ago he had conducted an investigation to see whether there was an inverse relation between the decline in tuberculosis and the rate of expenditure on hospital and medical services. No such relation had been discovered. He thought it important therefore that the public health service should concentrate on the basic conditions which affected the disease and keep a close watch especially on the general nutritional state of the people. The second aim of prevention was the isolation and removal of the patient. He did not think that the legal power under the National Assistance Act, 1948, for compulsory removal to an institution was of much practical value in cases of tuberculosis. The chronic ambulant infectious case who was homeless presented a problem. Local health authorities should consider the provision of special hostels, although these would be difficult places to manage and control. Alternatively, people living in houses with surplus accommodation might be persuaded to give rooms to such ambulant cases. Children in contact with open tuberculosis should be boarded out on the Grancher system. Some 600 London children were being cared for on this ground, mainly in residential nurseries and schools.

Sir Allen considered that mass radiography was best placed under the control of regional hospital boards provided that the local health authority advised on its best use. He believed that there should be arrangements for the *x*-ray examination of all persons in regular contact with groups of children; there were 30,000 such people in London. Another essential in prevention was good health-visiting in association with the chest physician.

Dr. G. W. H. Townsend (Buckinghamshire) discussed problems peculiar to counties and rural areas. In his experience the district councils had made little use of their powers under the Tuberculosis Regulations. Would the local health authorities do any better now that they had lost their functions in regard to treatment and retained only those of Section 28? He thought that welfare work confined to tuberculosis was time-consuming and should be combined with that for other conditions. Good co-operation between health visitors and welfare workers was essential. The tuberculosis service might also take a leaf from the maternity and child welfare book. Mothers at welfare centres waiting to see the doctor were learning all the time by lecture, film, or leaflet. At the tuberculosis dispensary waiting was just waiting, and here there was an opportunity for health education on welfare centre lines.

Dr. Stuart Laidlaw (Glasgow) said that more evidence was wanted on the relation of overcrowding and tuberculosis. In Glasgow they had found that the contact rate was twice as bad in 2–3-room houses as in 3–4-room houses. He disagreed with the attachment of the chest physician to the regional hospital board. The effect had been concentration on the curative and clinical aspects, and interest in the domiciliary side had waned. There was in Glasgow a waiting-list for sanatorium beds of 16,000, but no chance of admission unless the case was of special clinical interest. The M.O.H. had no power to enforce admission, so a day-to-day battle was in progress to get cases away from dangerous home conditions. Referring to Sir Allen Daley's point about hostel accommodation for ambulant cases, Dr. Laidlaw described how an empty ward in a tuberculosis hospital had been reopened as a hostel for 60 discharged patients who shared the catering and domestic work.

Dr. W. Alcock (Burton-on-Trent) speculated whether the decline in tuberculosis mortality was due to environmental improvements of the past 75 years or to a variation in virulence such as one saw in other infectious diseases. It was an inevitable conclusion that environmental and social betterment was fully responsible in this instance. He thought, however, that the factors of resistance, susceptibility, and acquirement of immunity still required much investigation, but suggested that when employment was high, housing good, and leisure time wisely spent tuberculosis would further decline.

Dr. K. Neville Irvine (Henley-on-Thames) said he would confine his remarks to three questions. (1) Should B.C.G. be given to selected cases or *en masse*? The Ministry of Health had decided on selection.

(2) Why was segregation required for six weeks before and after vaccination? It was wise to observe this rule in the interests of the prestige of this new procedure. If pre-segregation was impossible, they could vaccinate in the pre-allergic state. Likewise, if the Mantoux test six weeks after vaccination was not positive, there should be another test at 10 weeks before re-vaccination; some people were slower than others in conversion. When re-vaccinating after 10 weeks he advised a double dose. Failure to segregate after the first vaccination did no harm, but some cases might contract the disease before immunity was established, thus damaging the reputation of this form of protection.

(3) Was intracutaneous injection preferable to multiple puncture? This had been settled by the Ministry's decision to use the Copenhagen serum, which was specially prepared for intracutaneous injection. The dose should be doubled for newborn infants. Patients should be warned about the papule which might appear after two or three weeks and sometimes broke down to an oozing ulcer. Ultra-violet light cleared up such persistent ulcers with dramatic speed. Speaking of the groups to be selected, Dr. Irvine suggested that Mantoux-negative diabetics should be included as should Mantoux-negative cases in tuberculous families, especially those in contact with streptomycin-resistant cases.

There followed a general discussion in which a number of speakers took part.

CONFERENCE ON INFERTILITY

FAMILY PLANNING ASSOCIATION

The Sixth Annual Conference on Infertility was held in the Usher Institute, Edinburgh, on September 17 and 18, under the auspices of the Family Planning Association.

Mr. W. Selby Tulloch (Edinburgh) opened the first session with a paper on testicular biopsy in the infertile male. He described the technique that he found successful as an out-patient procedure; it was performed under local analgesia, 10% procaine being injected into the spermatic cord and into the scrotum at the site of incision. Suture of the tunica albuginea prevented haematoma formation. In none of his cases did the operation involve absence from work, nor did the patient complain of pain. He showed a series of photomicrographs illustrating the various biopsy findings in subfertile males. In the discussion that followed attention was drawn to the real danger of testicular damage resulting from the *x*-ray treatment of spondylitis ankylopoietica and to the characteristic absence of evidence of inflammation in biopsies from testes which had been the site of mumps orchitis.

Dr. Arthur Walton (Cambridge) spoke next on patterns of male sex behaviour. Characteristic behaviour was not sex-specific, since it was exhibited by the prepuberal male, might persist after castration, and in some species at least was normally exhibited by sexually excited females at all stages of the sexual cycle. The pattern was innate and showed the phenomenon of "drive," which increased in the absence of a normal outlet so that a substitute outlet might be found. Experimental work on rabbits had shown that the threshold of response and degree of completion of the pattern could be expressed as the product of two factors—the sex drive of the male and the excitatory value of the sexual object. That the motor pattern and accompanying reflexes could become highly conditioned to external stimuli was illustrated by a study of the behaviour of bulls during semen collection for artificial insemination; facilitation and inhibition were often observed. The applicability of these studies to human infertility problems was developed in the discussion. The importance of lack of sex drive as an infertility factor was demonstrated, among other things, by the finding of an intact hymen in 5% of "infertile" wives.

Dr. A. G. Oettlé (South Africa) read a paper, in conjunction with Dr. G. Van Drimmelen, in which he developed a theory of sperm quality based upon the known facts concerning the development and subsequent loss of the characteristics of motility, ability to fertilize, and ability to ensure completion of embryonic development. There were many gaps in our knowledge, and it was hoped that a consideration of the subject in this way might help to show where further work was needed to fill in some of these gaps. A lively discussion ensued, ranging over many aspects of reproductive physiology.

Ovulation

Dr. G. I. M. Swyer (London) described a method of treatment of anovulatory failure by the cyclic oral administration of stilboestrol and ethisterone. He reviewed the results of this treatment in 40 women in the reproductive years, consisting of 14 case in which the presenting symptoms were prolonged and excessive irregular uterine bleeding, 13 in which the periods were scanty and infrequent, or, if regular, found to be anovular, and 13 cases of secondary amenorrhoea of one year's duration or more. In the first group evidence for the re-establishment of ovulation was available in eight cases, and there were three pregnancies. In the second group the same number of successes occurred, but in the third group no successful results at all could be claimed. The discussion of this report centred around the problems involved in the establishment of the condition of anovulatory failure before treatment and the elimination of spontaneous cure—in other words, the difficulty of ascribing the results after treatment as being indubitably due to treatment.

Mr. Albert Sharman (Glasgow) read a paper on the re-establishment of ovulation post partum and after abortion. This was a preliminary communication of a wider investigation as yet incomplete. There had been five previous investigations on the re-establishment of ovulation, but all of small series of cases, and there were considerable discrepancies in the results. His own series consisted so far of 628 endometrial biopsies in 283 women post partum and 125 biopsies in 36 women following abortion. Seventeen patients had had more than 10 endometrial biopsies performed during the nine months following delivery. One patient had had 24 weekly biopsies. Mr. Sharman based on this material a full account of the re-establishment of ovulatory cycles and their relation to lactation.

Pelvic Endometriosis

Mr. G. Douglas Matthew (Edinburgh) discussed pelvic endometriosis in relation to sterility and showed that fibroids, metropathia haemorrhagica, fixed retroversion, and other conditions frequently coexisted. He considered the possible aetiological significance of social and economic conditions, and of prolonged oestrogenic stimulation without the respite of pregnancy. Diagnosis could be most difficult, especially since the severity of symptoms need bear no relationship to the extent of the disease; laparotomy, therefore, was the only certain diagnostic procedure and was recommended in all doubtful cases. Conservative surgery was the treatment of choice; if this was rewarded by pregnancy and recurrence followed, more radical measures could be adopted subsequently. In the discussion mention was made of the value of hysterosalpingography in the differential diagnosis of endometriosis from the late results of pelvic sepsis, and of the possible value of testosterone as a therapeutic test as well as in preoperative treatment.

Mr. S. Bender (Liverpool) drew attention to the existence of peritoneal pockets as a cause of sterility. Usually they resulted from pelvic peritonitis, which might or might not have caused tubal damage. Although tubal patency was almost always carefully investigated in cases of sterility, attention was seldom paid to the existence of a clear pathway between the ovary and the abdominal ostium. Obstruction of this pathway, or pelvic block, could be due to the presence of a pelvic pocket in relation to the abdominal ostium—easily demonstrated by salpingography—but it could also be due to the ovary being pocketed away from the general peritoneal cavity.

Disappointed by the results of other forms of treatment, Mr. Linton Snaith (Newcastle-upon-Tyne) said that he had been using oestrogens in the treatment of threatened and habitual abortion for the last two years. In threatened abortion, provided it was not inevitable, an initial intramuscular injection of oestradiol benzoate, 10 mg., was followed by oral oestrogen therapy. In habitual abortion oestrogens were given orally, starting a few days after the first missed period. There were 31 patients in this group, and in half of them stilboestrol alone had been used. So far the results were regarded as successful in 25 of these patients, other methods of treatment having previously failed in many of them. There was a surprisingly high incidence of toxaemia of pregnancy in these cases. Mr. Snaith reviewed the possible mechanisms whereby oestrogens could be of benefit, and concluded that there was no evidence that they did harm in pregnancy, while they might be beneficial, especially where "blighted embryo" in the early months of pregnancy was the cause of repeated abortion.

A full discussion followed, and the difficulties of assessing the results of treatment in habitual abortion, as well as its definition, were stressed. Despite their variations in treatment, nearly all who contributed to the discussion secured approximately 80% success. The random distribution of abortion sequences, as in the classical description of Malpas, had to be considered, and it seemed that only extensive controlled series could be expected to show the undisputed value of any therapeutic regime.

Fructose and Fibrinolysin

Miss Ursula Parsons (Cambridge) described the work she and Dr. T. Mann had done on the effects of testicular hormones on the formation of seminal fructose. Considerable variations in the seminal fructose concentration, both in the same and in different individuals, were found in man and in rabbits. In the latter, however, it was shown that castration was followed by a fall almost to zero in the seminal fructose, while the adminis-

tration of testosterone, both by implantation and by injection, was followed by the rapid return of the fructose to normal levels, from which it fell again on removal of the implant. Stilboestrol implants in intact rabbits also depressed the seminal fructose. Dr. MANN described how the fructose content of the castrated rat's prostate and seminal vesicles could be used as a sensitive indicator of androgenic activity—far more sensitive than the weight change—and it was suggested that this would provide a simple and satisfactory method for androgen assay. As little as 0.05 mg. testosterone could be detected by this means.

Mrs. CLARE HARVEY (Exeter) described a relatively simple method for estimating the rate of liquefaction of blood fibrin by seminal fluid. It was found that the time of liquefaction of a constant quality of fibrin was related to the fibrinolysin activity in a manner expressed by $\log C = a \log T + K$ where a and K are constants, C is the fibrinolysin activity measured in arbitrary units, and T time. A regression equation calculated for 99 points from 30 specimens of semen gave a very good fit for a further 110 points from 45 other specimens. The distribution of enzyme activity was found to be asymmetrical, most specimens having a total activity below 50 units. No correlation was found between enzyme activity, sperm motility, seminal volume, time of continence, and fructose content. The residual viscosity of semen was not closely related to enzyme activity, but it seemed probable that the citric acid, thrombin, and fibrinogen content might be at least as important as fibrinolysin activity in determining the final consistency of the seminal plasma.

At the close of the meeting the future of these conferences was discussed, and their continuation was thought to be desirable. It was also suggested that the time might be ripe for the formation of a society for the study of problems in comparative fertility, both from the animal and the clinical side. It was therefore decided to form a committee, of which Dr. A. Walton and Dr. G. I. M. Swyer were elected joint secretaries, the functions of which should be, in the first place, to arrange for a conference next year and, in the second, to consider and present before the conference plans for the formation of such a society.

THE PROBLEM OF RHEUMATISM

TWO-DAY CONFERENCE IN LONDON

The British Rheumatic Association, which was formed in 1947 to direct public attention to the needs of the rheumatic patient, to promote medical and social interest, and to stimulate research, arranged a two-day conference at Chelsea Town Hall on September 28 and 29. In connexion with the conference an exhibition was held at the adjoining Chenil Galleries, where some 15 firms had stands displaying preparations for the relief of rheumatic disorders, electro-medical apparatus, invalid furniture and transport, and devices for occupational therapy. There were also displays illustrating spa treatment, home and aftercare visiting, and industrial rehabilitation.

Lord HORDER, one of the vice-presidents of the association, who was in the chair at the opening of the conference, said that the B.R.A. was helping to make known the magnitude and economic importance of the problem of chronic rheumatism. Its liaison with the Empire Rheumatism Council, founded 15 years ago, was close and cordial.

Cortisone

DR. W. S. C. COPEMAN said that from the epoch-making announcement by Hench, Kendall, and others of the Mayo Clinic early this year it seemed evident that an abnormality of one of the constituents of the cortex of the adrenal gland was chiefly concerned in rheumatoid arthritis. Hench, working on the old observation that cases of rheumatoid arthritis got well during pregnancy, and on his own observation that this beneficial change occurred also in the course of certain types of jaundice, arrived at the conclusion that the common factor was the adrenal cortex. In 1947, trying out one of the cortical steroids which Kendall had isolated—compound E—Hench found that with large doses the whole disease process and activity, even in the most severe cases, could be reversed within a few days, though the condition relapsed as soon as the administration ceased.

Compound E was an extremely difficult substance to prepare, even in small quantities, and it had so far been impossible to synthesize it chemically. It was prepared at present by partial synthesis from ox bile, but sufficient quantities for adequate clinical trials would never be made available by that means. It had also been found that if adrenocorticotropic hormone, whose chief function was to stimulate the adrenal cortex, was injected a similar beneficial effect was produced, showing that patients could produce an adequate supply for themselves if forced to do so, but the nature of the lesion which prevented this in ordinary circumstances still remained unknown. This extract was almost as rare as compound E itself; there was a little of it in Europe, he believed, but much of it, so far as he could make out, was inactive.

The problem now to be solved was to produce compound E or any similar substance on a sufficiently large scale to make adequate clinical trials possible. At present only enough was available in the world to treat about 50 persons for a period of a few weeks. The discovery was likely to rank with insulin, and possibly with penicillin, but clinical use was still in the early experimental stage, and it should not be thought of as a practical treatment. The clinical results were manifest: stiffness, anaemia, and joint lesions cleared up; nodules disappeared; weight increased, in some cases so grossly that the patient had to be put on a reducing diet, and the blood picture returned to normal, though not immediately—"travelling," as Hench said, "on the same line, but not in the same train." A warning was necessary against false descriptions of compound E. Vitamin E with something else added had been presented by some vendors in America as "compound E," and therefore it was desired that the substance should not be given that description but should be referred to as "cortisone."

Dr. OSWALD SAVAGE, who, like Dr. Copeman, had recently seen this work in America, said that here again the research chemists had come splendidly to the aid of medicine, as they had done in the work on the sulphonamides and penicillin, and in work also on preparations such as stilboestrol. Those interested in the problem in this country would be greatly encouraged if they could see the excitement which this discovery had aroused in America. This was no mere flash in the pan. It was the result of years of patient research on the physiological side by Hench and his colleagues and on the chemical side by Kendall and his colleagues, both at the Mayo Clinic.

Rheumatic Patients in Rural Areas

Dr. W. S. TEGNER, secretary of the International League Against Rheumatism, said that patients in rural areas presented a twofold responsibility. The doctor must make an accurate diagnosis, and he must also plan his care in circumstances very different from those of a hospital clinic. Each type of rheumatism called for its own treatment, and, moreover, each patient was an individual and must be treated as such. The patient wanted to be told about his own disease and its management, and this was particularly important in the case of the rural patient. At the Mayo Clinic no patient went home without having listened to a series of lectures on his disease. The care of the rural patient was primarily, of course, the responsibility of the local doctor, who might call in a specialist if needed, but specialists in rheumatism were still rare and seldom accessible to the rural patient. Drug treatment of rheumatic conditions was ameliorative rather than curative. A form of treatment acknowledged to be of great value in the management of rheumatic disease and the prevention of deformity was physiotherapy, ranging from massage and exercises to complicated electrical treatment. Domestic physiotherapy was necessary for the rural patient. There was a danger that in modern physiotherapeutic advances it might be forgotten that for many years domestic methods, such as rubbing the part with liniment and applying heat by what would now be considered crude methods, had been highly successful. In the instructions given at the Mayo Clinic the patient, on being

discharged, was told of at least six different methods of applying heat apart from electricity. These included the hot water-bottle, the hot brick wrapped in flannel, the use of the flat-iron, and the like, some of which sounded antediluvian but worked well.

There was a good deal of mystery and misunderstanding about electrical treatment. Very often when a reference was made to electrical treatment no more was meant than the generation of heat. It might be that the rural patient was unable to obtain the ordinary forms of infra-red radiation or short- or long-wave diathermy as used in hospital clinics, but there were domestic substitutes for them which could be most valuable. Altogether, the rural patient presented a problem, an interesting one, which could be largely solved by personal interest and sound advice.

Dr. A. B. Williamson, administrative medical officer of the Leeds Regional Hospital Board, said that a scheme had been worked out for his region whereby nine peripheral clinics were or would be established at various industrial centres, and, as soon as possible, three others so placed as to serve rural areas. To these peripheral clinics, situated in hospitals, the patient could be sent for diagnosis, and if specialist advice was necessary he could be accommodated for a short time in one of a dozen beds. After diagnosis, treatment would be given in the department of physical medicine at the hospital or elsewhere. If treatment was not possible at the peripheral clinic the patient would be referred to the centres—Leeds General Infirmary and the Royal Bath Hospital, Harrogate, and there he might be treated as an in-patient for months. Out-patient clinics had been established in Harrogate, and for the ambulant type of case permission had been obtained from the Ministry of Health to take over a large hotel near the baths, where it was hoped to accommodate up to 160 patients.

Industrial Rehabilitation of the Disabled

The second half of the conference was devoted to the problems of rehabilitation. Air Commodore G. O. Venn gave an account of the progress of "Remploy Limited," of which he is executive director. Remploy Limited, until recently known as the Disabled Persons Employment Corporation, is an industrial undertaking operating factories as much on industrial lines as possible, and aiming to employ in productive work all men and women who are registered at an employment exchange as disabled and who cannot expect to obtain and hold work in open industry. The programme calls for 137 factories, 20 of which are to be specially for the tuberculous. At present the disabled are being employed in 62 factories, and nine more are in process of being staffed and equipped. Over 3,000 disabled are at work in the factories now established. A fair number of epileptics are being employed, also sufferers from diabetes, paraplegia, and cardiac conditions. In South Wales a large proportion of ex-miners suffering from silicosis have gone into these factories. The number of sufferers from rheumatism, including spondylitis, employed is 240. Air Commodore Venn said that they had had a fair amount of success, but they were a long way from covering their first costs. A "homework" scheme was being operated in ten districts, but the difficulty was to find a suitable product which could be made in the home and command a ready market.

Another contribution was by Mr. John Arthur, founder of Michael Works Limited, a woodworking factory, run as an ordinary economic unit, and employing 75% disabled labour. He said that a small proportion of disabled men could be reabsorbed in open industry, but many could not maintain the pace, and it became increasingly evident that small unit factories producing specially selected work were the best answer to the problem of the re-employment of the disabled. The first interview with the employee was the most important part of the rehabilitation process. At that first contact there must be established a positive assessment of the disabled man's remaining powers of working again and earning a living. He should be encouraged to think of what he could do as opposed to what disablement prevented him, in his own view, from doing. Once confidence was established the management must then see that the right job was found for the man.

REHABILITATION

A special clinic with demonstrations was given by Dr. Howard Rusk, of the Bellevue Hospital and the Institute of Rehabilitation, New York University, at the Royal Free Hospital on September 14, with Lord Horder presiding.

Dr. Rusk spoke of the enormous cost, in both wealth and happiness, which was incurred by a failure to secure proper rehabilitation after industrial and other injuries and illnesses. He gave a large number of figures illustrating this point, and then proceeded to demonstrate the various methods which he used. The cases in which he was principally interested were those of hemiplegia, spastic paraplegia, and various types of quadriplegia. If rehabilitation was to take its proper place, a correct diagnosis should be established in the first instance.

He went on to detail the various tasks which make up the routine of life. These tasks were set out on a form and each patient was provided with this form on entering the clinic. As the patient found himself able to complete his own toilet, move from a wheel-chair to bed, and from bed to a wheel-chair, and so on, the blanks on the form were filled in so that the patient could see his progress in pictorial form. So successful had this method of fostering a competitive spirit been, that by means of various mechanical methods even patients who were quadriplegic had been able to return to some method of earning a living and, even more important, had been rendered independent and able to look after themselves.

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL

The annual dinner of King's College Hospital Medical School was held at Claridges Hotel on October 1 under the chairmanship of Dr. J. H. Sheldon. The toast of the medical school was proposed in a witty speech by Dr. Wilfrid Oakley. In response the dean, Mr. Harold C. Edwards, referred to the difficulties of admitting students to King's. For some reason or other, he said, medical education was becoming very popular, and there had recently been 900 applications for 50 vacancies. In deciding who should fill the vacancies it was impossible to avoid disappointing some of the sons of King's men. But every attempt was made to assess objectively the qualities of the applicants. In spite of the legal separation between the hospital and the medical school they continued to work in close harmony. The toast of the guests was proposed in a felicitous speech by Dr. Sydney Thomson and responded to by Sir Hugh Cairns, who the day before had given the inaugural address printed elsewhere in this *Journal*. Sir Hugh said that his first acquaintance with King's was through the well-known textbook by Rose and Carless, which he read when a student in Adelaide. He compared this with Osler's great textbook—a source of questions in general knowledge. Sir Hugh said it was a pity that the National Health Service had to be so centralized, and referred sympathetically to the present difficulties of the general practitioner. Dr. Terence East, in proposing the health of the chairman, referred to his contributions on diseases of bone, anorexia nervosa, on the distribution of iron in the body, and now on geriatrics—not so boring as Cicero's *De Senectute*. In reply, Dr. Sheldon said that physicians often died of the diseases they treated, which was why he had become interested in geriatrics.

MIDDLESEX HOSPITAL MEDICAL SCHOOL

The annual dinner of students, past and present, of Middlesex Hospital Medical School was held at the Savoy Hotel on September 30 under the chairmanship of Professor E. C. Dodds. The chairman paid a tribute to the late Mr. Turner Warwick, with whom his own association dated back to the early 'twenties when Warwick was pathological registrar at the Bland-Sutton Institute. They welcomed that evening his son as senior Broderip scholar. Professor Dodds claimed for the Middlesex that it was "undoubtedly the most remarkable of medical schools." It aimed at keeping the basis of education as broad

as possible. There had been many criticisms of the medical schools of London that they were too narrow, but the benefactors of the Middlesex had indicated that it should be a school of research in addition to a school purely for the training of doctors. He believed that this broad administration, started by Sir Charles Bell Bland-Sutton and encouraged by Lord Webb-Johnson and others, had been well justified.

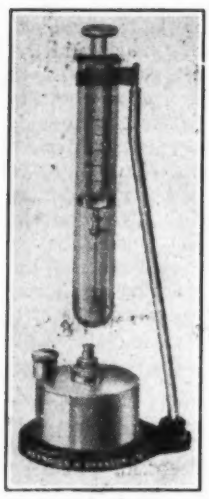
Dr. H. E. A. Boldero, dean of the school, said that looking back on the year, although it was the first year of the National Health Service and of the school's charter, he felt that extraordinarily little had happened. That was as it should be; changes should be slow and deliberate. He went on to refer to the retirement, due to take place on the morrow, of Professor John Kirk from the Courtauld chair of anatomy. Another figure they were losing, and one who had contributed greatly to the school in a different capacity, was Mr. R. A. Foley, the school secretary, who was retiring owing to ill-health. The school had appointed a woman as his successor—Miss Eileen Walton. Another Middlesex man of whom they were very proud was William Sladden. He qualified two or three years ago and was medical officer on an expedition to the South Pole. The expedition met with disaster, and Sladden's heroism and endurance under trying circumstances had earned high praise.

Mr. R. Turner Warwick, senior Broderip scholar, in responding to the toast of "The School," gave an account of athletic activities during the year. The evening ended with the drinking of the health of the chairman, proposed by Dr. G. E. Beaumont, who spoke of Professor Dodds out of a friendship which dated back to the time when Dodds came to the Middlesex as a student with "the valuable technique of passing every examination with distinction."

Preparations and Appliances

TEST-TUBE STERILIZER FOR SYRINGES

Dr. H. F. Barnard, Pathologist, Westwood Hospital, Beverley, E. Yorks, writes: Sepsis from an unsterile syringe procedure is not uncommon. The method here described offers a simple way to boil a syringe and handle it dry. It is speedy and can be used readily anywhere—for example, in the home—though it is appreciated in the surgery or ward.



A syringe of the glass plunger type rests in a glass boiling-tube, this being supported in a spring-clip stand over a spirit lamp. On lighting the lamp the water boils in 60 seconds and the syringe is surrounded by steam, whilst boiling water passes up the needle and barrel. Trials show that five minutes' boiling is sufficient. Normally a syringe is washed clean, but as a more searching test serum heavily infected with *Staphylococcus aureus* was allowed to dry on the plunger and in the barrel. After boiling for five minutes in the tube no growth was obtained from washings. Nevertheless it is important that the syringe should be used only for aseptic purposes.

When sterilized the syringe is lifted out by the handle, and the outside dries in a few moments. This avoids the risk of contamination spreading to the needle from the hand on a wet barrel. It is convenient to carry the syringe about in the tube after tipping out the water. If left in the tube the syringe remains sterile many hours. A useful protection of the needle-point is achieved in this method.

I would like to thank Mr. A. A. Ralph, of Reynolds and Branson, Ltd., of Leeds (the makers), for help in producing the apparatus.

Correspondence

The Innocence of Deans

Sir,—How stirring are the times in which we live. Never have learned doctors so bedevilled each other since the robustious days of the seventeenth and eighteenth centuries. The medical press is a free-for-all, with no holds barred and no non-combatants. The most innocent and peaceful observer who cautiously raises his head above the sandbags is liable to receive a shattering volley from all sides. So when Dr. Geoffrey Bourne (September 24, p. 704), a redoubtable slinger of verbal brickbats, is pelting Dr. H. E. A. Boldero with great gusto (in the hopes perhaps of winging another distinguished shadow he glimpses behind) a sudden association comes into his head and with one tremendous backhander he demolishes the whole damnable denomination of deans, men whose "whole outlook and training is one of honest and faithful subservience to an institution," incapable of defiance of authority.

Let authority take note of this testimonial to decanal innocence. So will we the better preserve in these difficult times the integrity of the institutions we subserve.—I am, etc.,

London, S.E.1. E. R. Boland.

Distinction Awards

Sir,—In your issue of September 24 (p. 704) Dr. J. W. Linnell's comments upon my letter (September 3, p. 545) suggest that he is under some misapprehension, arising in part from the condensation of my original letter to you in which I defined "postgraduate teaching hospital" so as to include "all those medical schools recognized as preparing candidates for the higher qualifications," while undergraduate teaching hospitals were defined as "those not preparing candidates beyond the qualifying examinations." The marks printed are the average of a few colleagues' markings and are included only as an indication of how the idea may be worked out.

I am careful to leave it to the Awards Committee to amplify and modify the scheme, and I suggest that every consultant should mark the Awards Committee's scheme in detail, that these marks should be averaged by a firm of accountants, and that the average markings should be binding on the Awards Committee. Thus Dr. Linnell—in common with every other consultant—would have the chance to record as many "0s" as he pleases, "to put down the mighty from their seat and to exalt the humble and meek." Others will join him in recording a "0" for "officers of academic medical societies," but some wished it to be included.

Another point obscured by the condensation is that while the averaged detail marking of Sections 1 and 2 would be final—each candidate scoring in each subsection the highest mark to which he is entitled—the marking in Section 3, "Publications," would not be greater than the averaged figure, but might be as little as 1%. I believe that a representative committee of each consultant group could mark each candidate on his application under this heading in a matter of minutes. Personally I shall be content if a man whose original work is outstanding scores as many marks for it as for "15 years of service on an undergraduate teaching hospital"—we are required to assess Distinction—but once again Dr. Linnell may put down what figure he likes. His statement that the scheme "attaches no value to such vexatious and intangible considerations as clinical acumen and judgment, or operative skill," is surely frivolous. If a consultant's senior hospital appointment and the years of service he has given to that post and to others leading up to it are not a criterion of his "clinical acumen, judgment, and operative skill" then we must indeed abandon hope of solving this problem, for every appointments board before whom he has appeared has sought to assess, after full consultation and deliberation, just those things.

The Awards Committee is required to carry out certain duties which were defined by the Spens Committee, approved by the profession, and then—and only then—passed into law. Apart

from abstention, the time has gone by when we can do other than assist the committee in their thankless task. I have sought to put into words an idea which may prove helpful. The Awards Committee decides what factors contribute to the idea of distinction, and the consultants as a whole decide, democratically, what marks are to be attached to those factors.—I am, etc.,

London, W.1. FREDERICK RIDLEY.

SIR,—Those of us who have read and admired the writings of Dr. F. M. R. Walshe appreciate the courage, wisdom, originality, and sincerity of his contributions to medicine. He is an acknowledged leader in thought, fittingly recognized. Yet in spite of this, or perhaps because of it, we see him running counter to the controlling political and academical authorities of the day. Surely he must be given the distinction of being called a "reactionary," a "difficult fellow," or, by those who fear him, "naughty," for these are the terms in which we honour the leaders of our time. Mr. Winston Churchill has been so distinguished in the House.

Let Dr. Walshe not fear that he is without support from graded specialists, for many of them now realize that their previous failure to interest themselves in the nomination of, and voting for, political and academical leaders has cost them very dearly. The members of the profession voted with a solidarity previously unknown against this set-up, but that was when few realized the enormities now beginning to be revealed to them. I venture to suggest that if the planners had clearly shown their designs, and the humbug attaching to them, a far greater solidarity against them would have resulted which would have been maintained in spite of the leaders; and the public would have benefited.

Dr. Walshe (September 17, p. 649) states, "The power of money is great." He realizes that local influence is to be used and is feared, that the awards are in the power of the planners with sycophants as satellites. These hate criticism and have designed their set-up to keep out the "difficult fellows." They are steadily acquiring a dictatorship which threatens not only the "distinction awards" but the very liberty of the doctor. The writings of the workers will have to be submitted to powerful dictatorial overseers who will so secure their "notice": failure to do so may mean rejection or even a blasted career. At the moment one of our leading surgeons can state, "I personally suspect the man with huge figures and a negligible mortality of being a surgical spiv," but how long will the critic of statistics be so tolerated? Canvassing for votes with intimidation, or even instruction, for high distinction or office in the profession already exists, and woe betide the "difficult fellow." As I overheard the conversation, "He's probably the best man we have on the staff; but why, why, why does he keep that imp on his shoulder?" Criticism, however justifiable, of the scientific or political activities of the powerful—the life essence of a progressive profession—will become difficult—yes, and hazardous—to the career of the critic.

Speaking as a radiologist, prior to this service radiologists kept their liberty by earning their living with their own units to the benefit of their patients and the Exchequer and with credit to the profession. Their private apparatus, at a time when the country is financially embarrassed, has to all intents and purposes been scrapped, while the hospitals are clamouring for more and more equipment (though probably adequate to do reasonable requirements) and the manufacturers with stores filled with units await "instructions." By the time the units are supplied they will be out of date. But even to mention such matters may jeopardize a "distinction award."—I am, etc.,

Birmingham. JAMES F. BRAILSFORD.

Medical Education

SIR,—There were several most interesting articles in the educational number of the *Journal* (September 3) on aspects of medical education, and although some time has elapsed since they appeared I hope I may be allowed to comment on them. I feel that this is the more needful in that they imply that there is only one kind of approach to medical education, an approach which might be summed up as more courses, better courses, or linked courses. I shall confine myself to two lines of criticism.

The first criticism is of all this talk about scientific method. It seems to be hoped that, by reading scientific textbooks and attending systematic courses of lectures in different branches of science, scientific method will somehow be inculcated. Such courses are doubtless important for the student of science, but surely he does not acquire scientific method from them. They are aids in dealing with actual problems of science and sometimes may suggest them. But scientific method surely starts with the recognition of a problem and consists in the isolating of it from irrelevances. It is in fact a kind of interrogation in which the framing of a question is of great, possibly of paramount, importance. Its affinity with clinical examination is obvious, but there is no closer relationship between scientific method and clinical examination. The objects of each are too diverse.

While it is an attractive ideal that every doctor should be trained in scientific method, I venture to suggest that it is neither an essential nor even a possible one. The problem for medical educationists therefore resolves itself into that of how much of the enormous corpus of knowledge in biology and its derivative sciences should be insinuated into medical students.

The second criticism refers to the question of skill in medicine. Professor W. Melville Arnott (p. 497) asserted in his address that medicine is essentially a science—"is an art only in so far as the term means human skill." An art in this sense, and in most senses, is capable of being taught to a very considerable extent. In music and the pictorial arts this is recognized by the establishment of schools for the purpose. It was therefore disappointing to find in an address on reform in medical education no reference to attempts to improve "human skill" in the practice of medicine. Surely it is not considered that the human skill of the newly qualified graduate is as high as it should be. There are certain aspects, notably in the practice of asepsis, where nursing education is superior to medical.

One is tempted to develop this theme further, but I shall content myself with the suggestion that in a revival of apprenticeship lies the most hopeful path for progress in medicine. Such an apprenticeship, served mainly in hospital and begun early in the medical curriculum, not left to an intern year at the end, will itself enable the student to learn from his lecture courses. Such close acquaintance with the material of the subject studied has been the condition determining the progress of the whole scientific movement; it seems the most likely method of developing a genuinely scientific outlook in those medical men temperamentally capable of it. But it will require all the hospitals in this country to provide such an apprenticeship. The persistent separation of teaching hospitals from all others would have to be abandoned and some type of union of boards of governors with regional hospital boards set up. On other grounds, mainly administrative, this has already been mooted. One may hope that it will be speedily achieved.—I am, etc.,

Heswall, Cheshire. DAVID WILKIE.

Teaching of Physiology

SIR,—In discussing the imperfections of the practical training in physiology (September 3, p. 502) Professor G. W. Pickering makes the following statement, "Classes in mammalian physiology in Great Britain will be difficult to organize so long as they are based on the cat or dog, uncommon and expensive animals the use of which is much hedged round by restrictions," and he goes on to cite the example of Adelaide, where wild rabbits are used which are tough and cheaply trapped. One is left with the feeling that the problem of animal supplies in this country exists only because of the lack of resource on the part of British physiologists in failing to discover and trap some suitable British mammal. Might I correct this impression by some brief comments on the statement which I have quoted above?

1. Expense is not the deciding factor in making a choice between cats and rabbits. Current prices are: rabbits, 10s. ; cats, 10s. to 15s. Even Australian rabbits imported would not be likely to be much cheaper.

2. Uncommon is not the best word to describe animals whose occurrence is indicated by figures taken from the report of the Sheffield branch of the R.S.P.C.A. as reported in the *Sheffield Star* (June 15, 1948). According to this, during the previous year 10,531 cats and 5,777 dogs were destroyed in Sheffield (pop. 476,360). If these figures are typical for the whole country about 1,000,000 cats and 500,000 dogs are destroyed annually in Great Britain.

3. The restrictions mentioned by Professor Pickering are hardly relevant, since the use of any vertebrate (except the human being) is subject in this country to restrictions very similar to those on the use of dogs and cats, and these restrictions would certainly prohibit such interesting experiments as Professor Pickering describes in Australia. On the other hand the use of decerebrate cats is not hedged around by these restrictions, and Professor Pickering must know of the standard textbook (*Mammalian Physiology*) of Liddell and Sherrington, using decerebrate cats.

4. No other animal, human or otherwise, known to me and available in this country at any price can entirely replace the dog and cat for teaching and illustrating many of the fundamental principles of physiology, and if Professor Pickering knows of any such animal I and doubtless other physiologists would be grateful to learn about it.

The real obstacle to improving our mammalian physiology courses has been missed by Professor Pickering. It is simply to make available a tiny fraction of these odd million cats and dogs, unwanted and of no commercial value. The problem is ultimately to convince the ordinary kind-hearted and animal-loving citizen that these animals could be of enormous value to medical training and medical progress and, further, that killed individually by trained physiologists under conditions carefully supervised by the Home Office these unwanted creatures are likely to meet a more merciful end than by mass extermination in lethal chambers.

The physiologists, who might be thought to have a not completely unselfish interest in the matter, have hitherto failed to get their point of view accepted by those in authority, and what is needed is a wider recognition of the problem by those interested in medical education but not directly concerned with the teaching of physiology. It is, therefore, a great disappointment to me to find such a lack of appreciation of the problems of British physiologists by one so closely in touch with physiology and so deeply concerned with the whole problem of medical education as is Professor Pickering.—I am, etc.,

Sheffield. D. H. SMYTH.

Thymectomy in Myasthenia Gravis

SIR,—Mr. Geoffrey Keynes's account of his 155 thymectomies (September 17, p. 611) will have been widely read with deep interest. The successful accomplishment of this major operation on so many patients implies surgical skill of the first order. When we turn to the results we are naturally disappointed, as Mr. Keynes must be, that it is not yet possible to select those most likely to benefit from surgery. It seems that a thymoma is unfavourable, but we are otherwise in the dark.

The significance of this big experiment is so important that we must be wary of any possible flaw in its interpretation. A comparison of neostigmine dosage before and after the operation is a useful criterion when the difference is great—Mr. Keynes's groups A and B—but in those with only slight improvement it may well be falsified by the patient's attitude to the drug. For instance, a patient advised to reduce the dosage, and sometimes to stop taking the drug because it is thought by her advisers to be dangerous, will obey and lead a less active life or, more often, make a false return to follow-up inquiries. This is no idle speculation ; I know it to be true of some patients.

A second difficulty in assessment concerns the time lapse allowable between the operation and the beginning of improvement. Surgery must surely set itself reasonable limits in this respect. It is difficult to give credit to the operation for a result that is not seen for, shall we say, three months. This time lag is not made clear by Mr. Keynes.

Although I have been unfortunate enough to see six failures in consecutive thymectomies in my patients I am certain that remarkable and unusual remissions have taken place in many cases. Dr. Viets, whose 250 patients at his Boston clinic make him the most experienced student of this disease, tells me that he is satisfied that surgery has been followed by rapid improvement in some patients he had known for years and who had shown no previous good remission.

We are still entitled to speculate on the cause of the more numerous failures. Can it be that myasthenia gravis is a label covering a number of disorders of the myoneural junction? Every functional unit of the neuromuscular system has its own varied pathology—cortex, pyramidal tracts, anterior horn cells, and peripheral nerves are vulnerable in their several ways. Is it not, *a priori*, likely that the myoneural junction, susceptible to curare and in "myasthenia," can be impeded in more ways than we know? Sheldon and Walker (*Lancet*, 1946, 1, 342) have shown that the condition I have called acute thyrotoxic bulbar palsy, in which neostigmine response is striking, can be cured by thyroidectomy.

In future assessments we would do well to remember that recovery from a severe myasthenic state, however striking to behold, is not in itself a reliable criterion. Experienced workers in this field will agree that remissions are more common in the acutely afflicted than in those with a mild chronic course. We need an analysis of results in patients known for their previous even behaviour. Such figures, which I hope Mr. Keynes can abstract from his records, would give a better idea of the effect of thymectomy than we could ever obtain from a large unselected series.

Mr. Keynes's stimulating lecture raises another subject. Clinical and biochemical studies of this large group of thymectomized persons must surely yield some clue to the function of the thymus. We may hope that this new operation will advance our knowledge of this organ, just as the work of Reverdin and Kocher helped to open up thyroid physiology.—I am, etc.,

London, W.1. L. P. E. LAURENT.

Gravitational Ulcers of the Leg

SIR,—My paper on the aetiology of gravitational ulcers (August 27, p. 458) was based on 270 patients seen personally in the skin department of the Leeds General Infirmary. The series included every patient that I saw with this condition during two and a half years, and for this reason the term unselected was applied. These patients had ulcers present for a period varying from a few weeks to many years. A number of them had been referred before treatment by surgeons on the staff of the infirmary and from the varicose-vein clinic. The series seems to me to be representative, and my findings are not markedly different from those of Bauer working in a surgical clinic.

Dr. H. S. Russell's description (September 10, p. 598) of my series bears no relation to the facts as given in my paper, and his feeling that I have "seen the failures and should study the successes" before coming to a conclusion is as unjustified as it is unreasonable. My paper was concerned with the cause and not with the treatment of these ulcers. Hence, of those patients whose varicose veins had been injected, only those in whom this treatment seemed to be the direct cause of their chronic venous stasis were mentioned.

Mr. H. J. Croot (September 17, p. 654) does not quote me quite completely. I wrote, "The concentration on treatment of superficial varicose veins in patients with venous stasis is neither rational nor useful. . . . " The point I wished to make was that if varicose veins are present in a patient with venous stasis with or without ulceration, all too often treatment is concentrated upon them and not upon the fundamental cause of the condition—namely, a deficient venous return from the whole limb. While I am perfectly aware that treatment of such varicose veins may in a few carefully selected cases benefit the ulcers, yet in others injection of such veins may intensify the chronic venous insufficiency already present, possibly by causing thrombosis, not only in the superficial varicose veins but also in the third system to which Mr. Croot refers.

The problem of aetiology must be solved before treatment can be rational, and more about both, I feel sure, will only be learnt by co-operation between surgeons, anatomists, pathologists, radiologists, and physicians, and only if the broad view of the circulation of the lower limb taken by your annotator (August 27, p. 480) is adopted.—I am, etc.,

Zurich. S. T. ANNING.

Transmission of Syphilis

SIR,—Dr. A. O. F. Ross (April 10, 1948, p. 691), writing on the transmission of syphilis, reached the conclusion that "the advice that should be given to an adequately treated male is that he should not attempt to procreate children until five years after the date of infection." A case of a man and his wife seen recently by me seems to confirm this.

A woman, aged 27 years, was referred here late in pregnancy with two positive blood Wassermann reactions, which had been taken as routine—the second, of course, to confirm the first. She had no signs or symptoms. About a year previously, while living elsewhere, she gave birth to a baby, of whom her husband was the father, who developed a rash on its palms and soles soon after birth and who died of "pneumonia" when two months old. There can be little doubt that the child had congenital syphilis. The mother had not had a blood Wassermann reaction done during this pregnancy, which was her first.

All the facts of the husband's history have been confirmed. The diagnosis in his case was primary syphilis, sero-negative; on March 20, 1944, and on the following day dark-ground examinations of serum expressed from the sore in the penile sulcus were positive for *T. pallidum*. His blood Kahn test on March 20, 1944, was negative, and the Wassermann reaction on the cerebrospinal fluid was also negative three months later. He had adequate treatment for a year, and subsequent blood Wassermann reactions and Kahn tests were all negative.

He returned to England after military service on December 1, 1945—i.e., about one and three-quarter years after infection. He became engaged to the girl who is now his wife in 1946, when he had intercourse with her for the first time; they were married later in that year. (This story is confirmed independently by the husband and wife.) Her baby was born in 1947, and, as I have said, this baby died aged 2 months of probable congenital syphilis.

The wife told me that she had never had intercourse with anyone except her husband and that there was no previous family history of syphilis. She is one of six children, all living, as are her father and mother. She was an in-patient in a sanatorium for eight months in 1942; the medical superintendent writes me that she had "a tuberculous pleural effusion. There was no suggestion at that time of her having syphilis, so no blood Wassermann reactions or Kahn tests were done." The husband's blood Wassermann reaction and Kahn test were both negative on two occasions a few months ago.

Of course, we can never disprove that the wife had not had syphilis before she was married, but this is very unlikely, and the probability is that she was infected by her husband.—I am, etc.,

Barry, Glam. PHILIP SIMON.

"Acute Abdomen" in Diabetes Mellitus

SIR,—Though one reads of the "acute abdomen" of ketosis[1] and sees it referred to as a differential diagnosis by Zachary Cope,[2] it is not often that one is confronted with this problem.

On September 12 a man of 24 years was brought to hospital as an acute abdominal emergency. He was writhing in agony with abdominal pain and continuously crying out to be given something to relieve his pain. The history was that 18 hours previously, following a bout of vomiting during which, in the course of an hour, he vomited about five times, he was seized with abdominal pain. The pain persisted and had increased in intensity since the onset. The description given by the patient of the pain was that it felt as though he was "breaking in two." He was sure it was not a colicky pain. The pain was confined to the abdomen. He was quite definite that the vomiting had preceded the pain. Lawrence[3] mentions this latter point as an aid to diagnosis. It transpired that the man had been a known diabetic for three years and was on 54 units of insulin daily, with a calorie intake of 2,500 a day on a line diet regime. He had run out of insulin three days prior to admission, but continued to eat and had not made any great effort to obtain a further supply of insulin.

On examination, he presented the picture of an acute abdominal catastrophe, with a drawn, anxious, pale look, a dry, coated tongue, subnormal temperature, and a pulse rate of 120 a minute. There was a strong smell of acetone from his breath. The abdomen was held rigidly but with persistence, and between paroxysms of writhing it was apparent that there was no true rigidity. No definite tenderness could be elicited, peristalsis was heard evenly in all areas, liver dullness was present, and rectally no abnormality was discovered. The urine contained a large amount of sugar, acetone, and acetoacetic acid. The urinary chlorides were 1 g. per litre and the urinary diastase was 2 units. While being examined the patient complained of severe thirst, and when permitted to do so drank 1¼ pints (850 ml.) of water without pause.

Despite the picture of acute catastrophe, it was not felt that an acute abdomen of so many hours' duration could be possible with so little in the way of definite physical signs, and it was considered safe to give morphine ¼ gr. (16 mg.). Immediate treatment of the hyperglycaemia was instituted, and an intravenous saline drip commenced. Quite soon afterwards the patient quietened down, showed the typical air-hunger respiration of ketosis, the pain disappeared, and the abdomen became flaccid and free of tenderness in all areas. He made an uninterrupted recovery once his diabetic condition was stabilized.

It is regretted that in the urgency of getting the patient controlled no blood estimations were done. It is felt that the nature of the abdominal condition was comparable with that seen in uraemia. I know of no explanation of the "acute abdomen" in ketosis, and I would be very interested to hear of one.

—I am, etc.,

London, S.E.5. M. GLICK.

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1 *British Surgical Practice*, Vol. 3, 1948, p. 250, London.
2 Cope, Z., *Early Diagnosis of the Acute Abdomen*, 1946, London.
3 Lawrence, R. D., *The Diabetic Life*, 1944, London.

Pavlov and Conditioned Reflexes

SIR,—Pavlov studied conditioned reflex salivation. If one generalizes by using the word "behaviour" one may bracket in two different ways and say either that he studied conditioned behaviour or that he studied conditioned reflex behaviour. These generalizations are not identical, but many writers in referring to Pavlov's work appear to believe that they are.

Most of Pavlov's concepts appear to me to be labels lacking all reference to process. It enlightens no one to be told that when King Alfred let the cakes burn his sense of smell was inhibited at the time by virtue of inhibition.—I am, etc.,

London, E.13. W. THOMSON BROWN.

Treatment of Ringworm of the Scalp

SIR,—The search for an alternative to *x*-ray epilation of the scalp for the treatment of tinea capitis continues, and the recent article on this subject by Drs. H. Haber, R. T. Brain, and Mr. J. W. Hadgraft (September 17, p. 626) shows no doubt a step in the right direction. Yet it seems that due warning about the relative ineffectiveness of their salicylanilide in carbowax preparation when compared with *x*-ray epilation was not given. The practitioner may therefore be inclined to the belief that an alternative is almost at hand.

In the first place it would seem very wrong to utilize cases of *Microsporon felineum* infection of the scalp to prove the efficiency of any local application. Such infections usually undergo spontaneous cure within months even in the absence of any severe inflammatory reaction, and in their group of 20 cases (including seven showing an inflammatory reaction) a 75% cure rate after anything up to 14 weeks' treatment is very little better than one would expect with no treatment at all.

The single case of *Trichophyton sulphureum* infection did not, of course, respond to treatment. We are therefore left with an uncontrolled series of 6 cases of *Microsporon audouini* infections of the scalp. Unfortunately the duration of infection in each case before treatment was started is not stated. From a study of scalp ringworm in Northern Ireland it has become apparent that about a quarter of all cases of *M. audouini* infections of the scalp undergo cure in less than 6 months if left entirely without treatment (91 out of 374 cases in one localized epidemic. Facilities for *x*-ray epilation of this number in addition to cases from a large epidemic in a second centre were not immediately available, and these cases had

to be kept under surveillance until facilities became available.) In addition, a number of our cases have been successfully treated by manual epilation under Wood's light at weekly or twice-weekly intervals. Manual epilation with forceps can be little better than scrubbing with a nail brush every morning for weeks on end. When viewed in the light of these facts four successful results from six cases is not very encouraging.

A trial of a number of local applications has been made by us in some cases of tinea capitis. Fourteen cases have had a salicylanilide in carbowax preparation with instructions to "rub in thoroughly night and morning to the entire scalp after cutting the hair short." The results are still only provisional, but they are sufficiently discouraging for us to have abandoned use of this particular preparation except for purposes of completing the clinical trial. Of the 14 cases no less than 4 have so far developed a severe contact dermatitis (after 2, 2, 8, and 8 weeks' treatment). Actually this brought about cure in all four cases—but the method is not to be recommended! Dr. Haber and his colleagues do not mention the possibility of local reactions.

Articles such as the one under discussion are of certain theoretical value so long as the impression is not left that local applications alone have already an important place in the treatment of scalp infections due to *M. audouini*. It is often only with difficulty that one succeeds in obtaining permission from the patient's parents (and the family doctor) for *x*-ray epilation. The only effective way to prevent epidemics is to epilate cases immediately they are seen. Failure to do this resulted in our 374 cases in one small centre. A satisfactory *x*-ray epilation carried out by an experienced *x*-ray therapist results in freedom from infection within 4–6 weeks and allows the child to return to school, etc., without being a potential danger to the community. No effort should be spared to make these points with practitioners, who, after all, see the patients first.—We are, etc.,

J. Martin Beare.
Ivan H. McCaw.

Belfast.

Massage with Adrenaline

Sir,—My attention has recently been called to a circular which is being sent "to the Medical Profession only," claiming that a proprietary preparation alleged to contain adrenaline, and exhibited by inunction, has beneficial results "in all forms of rheumatism." The circular is plausible enough at first sight, for it suggests that adrenaline stimulates the production of Kendall's Compound E; and at a time when the dramatic outcome of Hench's work with Compound E is familiar to your readers some of them may be led to prescribe the preparation advertised in the circular.

Nobody would wish to decry the value of physiotherapy in rheumatic disease. But I feel that a few words of caution may not come amiss to those who are not actively engaged in clinical endocrinology. (1) The quantity of adrenaline in the preparation is not stated. (2) It is doubtful how much adrenaline is absorbed by inunction, and whether the effect of adrenaline so absorbed is more than transitory. (3) There is no evidence that adrenaline absorbed through the skin stimulates the production of Kendall's Compound E.

In brief, this preparation only advertises itself by a series of conjectures and hypotheses, and I should advise medical men to steer clear of it.—I am, etc.,

G. L. Foss.

Bristol.

Hypnosis in Treatment

Sir,—Dr. K. M. Hay (September 17, p. 653) writes, "The mind is then influenced on the feeling level and to a lesser degree on the intellectual level by the hypnotist: in effect we may say that the hypnotized subject is to a great extent depersonalized." For psychologists and psychiatrists depersonalization means a condition in which the subject is continuously compelled to doubt the reality of his own experiences. Lest we should be accused of restricting to our own use a word which has previously been used in a wider sense, may I quote the passage in which this term was first used? "Cet état dans lequel le moi sent ses actes lui échapper, et lui devenir étrangers, j'appelerai une alienation de la personnalité, ou dépersonnalisation" (Dugas, L., *Rev. Philosoph.*, 1898, **45**, 501).

This word, referring as it did to a syndrome with which psychologists and psychiatrists had long been familiar, has since been freely used by French, German, British, American, Spanish, and Italian writers. It has done good service for half a century in this sense. To use it in another would be to debase its value and lead to confusion.—I am, etc.,

D. S. Macphail.

London, S.W.3.

Essential Hypertension in Pregnancy

Sir,—Professor J. Trueta (September 17, p. 650) has forestalled me in replying to some of the points mentioned by Mr. R. H. Paramore in his letter (August 27, p. 486), but I should like to add something by way of comment on the latter's second two paragraphs.

Mr. Paramore explains the re-establishment of urinary flow under spinal anaesthesia as consequent upon the fall of blood pressure. Hingson, however, whose experience in this particular field is probably unique in its extent,[1] finds that it is often necessary to withdraw the spinal anaesthetic for a while and to give the patient ephedrine in order that the anuria may be relieved—i.e., that urine begins to be passed as the blood pressure rises and not as it falls. He is not averse to this phenomenon being explained as due to a differential action of the sympatheticomimetic drug, the renal vessels being less responsive than certain others to it, so that the general rise of pressure sends more blood through the former.[2] Such differential action is also the basis of the "order of sacrifice" which was advanced in 1947 by Professor Franklin[3] and has since been supported by further, as yet unpublished, experimental evidence obtained by him and by others, myself among them.—I am, etc.,

John Sophian.

London, W.1.

References

1 *See* Lull, C. B., and Hingson, R. A., *Control of Pain in Childbirth*, 3rd ed., 1948, Philadelphia, and subsequent papers by Hingson *et al.*
2 Hingson, R. A., 1949. Personal communication.
3 *St. Bart's Hosp. J.*, 1948, **52**, 30.

The Backward Child

Sir,—The school holidays just passed have brought the usual mass of school-children for advice because of school failure who are found on investigation to be backward because of a specific difficulty in reading and spelling depending on cross laterality of hand and eye dominance. The most serious cases seem to be the left-eyed and right-handed, but left laterals, with left dominant hand and eye, are only a little less serious.

This form of word-blindness is responsible for so much apparently unexplained school failure—the children "who could do better if they tried"—that it merits much greater attention. The condition is well recognized. It has been described by Sir Henry Head in his book on aphasia, Sir Cyril Burt in *The Backward Child*, Professor Schonell in *Backwardness in the Basic Subjects*, and in many papers in the journals. In America a great deal of research has been done on it. It is essentially a physical problem, but, as failure and frustration are gradually felt by the child, secondary psychological effects appear. Then loss of confidence, feelings of incapacity and social inferiority, and sometimes wild behaviour and even delinquency follow. Games needing co-ordination of hand and eye also suffer, and bring an added feeling of futility. These secondary symptoms usually develop when the child passes 10 years and begins to be self-conscious and to compare his attainments with his own ambitions and the achievements of others. Until then he has usually just been called lazy, or stupid, or inattentive, or "not trying," and he accepts the criticism.

The remedy is to ease educational pressure on reading and writing, to avoid criticism, to make the education as far as possible verbal instead of graphic, and to increase self-confidence through activities which give success. The difficulty usually fades at adolescence, and if the education has been kept at a reasonable level and discouragement avoided there should be little trouble after that.

The essence of prevention is to recognize the condition when the child is learning to read and give skilled tuition then, remembering that the child, however intelligent he may be, will be slower in learning the use of the written symbol than his fellows but that he will, with care, ultimately master it.—I am, etc.,

London, W.1. WILLIAM MOODIE.

Old Age

SIR,—Your correspondent Dr. J. Rushworth Lund (October 1, p. 758) complains of the number of old people who have grown selfish and useless, and suggests that as they eat food and require attention they should be quietly put to perpetual sleep.

This is a brutal proposition. There are, of course, selfish old people, but they are the exception rather than the rule. I could show Dr. Lund large numbers of the aged who are unselfish, kind, and thoughtful, who still do good work, and who are loved by those with whom they come in contact. I would remind him there are plenty of examples of selfish, useless, middle-aged people, and the same applies to the young. Are they all to be exterminated?

I do not know to what age group Dr. Lund belongs. Obviously not the aged. I hope he has many years of useful work before him. Later in life he will probably look a little more kindly at the old people. So many of them have worked hard and done so much good that they deserve some consideration at the end of life. I trust he will get no support for, or sympathy with, his perfectly horrible suggestion.—I am, etc.,

Hove, Sussex. L. A. PARRY.

SIR,—Dr. J. Rushworth Lund's letter (October 1, p. 758) on the above topic carries with it many dangerous implications which if not refuted may still further damage our society already burdened with the false concept of atheistic materialism. Surely the experience of the last ten years should now indicate to any sensible person how shallow such a concept of life really is.

Has not this materialist concept of life crumbled into dust and ashes in the very sight of those most anxious to build it up?

Old people should never ask themselves, "What use am I in the world?" Nor indeed should anyone. As for sons and daughters unable to marry, has Dr. Lund never heard of charity, the greatest of all the virtues? When a person's natural rights are voluntarily surrendered in the interests of charity that person is living on a very much higher sphere than the person who in similar circumstances insists on the exercise of his natural rights. As to segregation and euthanasia, are these remedies really compatible with the dignity of the individual? Has the individual no supernatural destiny? And who without just cause can take the life of another individual, which, I suggest, Sir, belongs to God and to God alone?—I am, etc.,

Barnsley, Yorks. EDWARD D. JONES.

Paddington Green Children's Hospital

SIR,—I would like to add a word to Dr. D. W. Winnicott's letter (September 24, p. 711). The first post I held in London was as houseman in Paddington Green Children's Hospital fifteen years ago. Since then I have never worked in a more happy hospital nor one in which the individual counted for so much. Everybody knew everybody, from telephone girl to senior physician, and the hospital was a happy, highly efficient unit with a high sense of duty and individual responsibility. It has always seemed to me that this small children's hospital was in its way among the very best of its kind.

In the new order of things it is I suppose inevitable that these things will occur, but is it sufficiently appreciated by the public that they have now one less hospital in their area to serve the local needs, and by the medical profession that it leads to termination of appointments of members of the staff, who have usually given many years' honorary service to such hospitals, without redress and with very little thanks? This mantis-like union of small hospital with large is apparently unhealthy for the patients and medical staff of the smaller partner—the larger, in a few recent instances, digesting bricks and mortar satisfactorily while unable to assimilate the human portion of the diet. In the closing down of Paddington Green Children's Hospital the population of the area has suffered a personal loss, as have also those of us who remember this hospital in the past.—I am, etc.,

London, S.W.1. F. DUDLEY HART.

SIR,—Dr. D. W. Winnicott (September 24, p. 711) has done a great public service in bringing to light the facts concerning the closing of Paddington Green Children's Hospital. It is indeed a tragedy that such an institution, second only to Great Ormond Street in efficiency, can be so quietly planned out of existence. By some mischance St. Mary's was allotted two children's hospitals, whereas there are two other teaching hospitals in the North-West Metropolitan area who have none. It would seem a simple matter to arrange a transfer, and it would save the Ministry of Health £10,000, which is the estimated cost of transforming a 50-bed children's hospital into an adult hospital with half the number of beds. A petition signed by 8,000 mothers, protesting against the closure, has this week been presented to the Minister. Perhaps this plea may prevail where logical argument has failed.—I am, etc.,

London, W.1. MASSEY DAWKINS.

SIR,—Dr. D. W. Winnicott (September 24, p. 711) is to be congratulated on making known the regrettable intention of St. Mary's Hospital Board to close the Paddington Green Children's Hospital and also for stating his views so fairly and so pointedly. Furthermore, I feel absolutely certain his opinions are those of everyone who has had the privilege and joy of serving such a splendid institution and would be strongly supported by countless mothers in the district, and further afield, who have themselves been kindly treated there or regularly take their own children for treatment there in preference to the less personal out-patient department of the general hospitals in the area.

Having been fortunate enough in the course of my paediatric training to have held an appointment at this worthy and happy hospital, I would like to state that Dr. Winnicott's remarks are in no way exaggerated. In fact the personal and happy atmosphere that prevails is one of the outstanding characteristics of the hospital and is quite unique. The decision to close the hospital could only be made by persons ignorant of this fact and of the tremendous amount of work done by the hospital which would have to be diverted to the already crowded, less specialized, and less personal casualty departments of other hospitals.

There can be little doubt that whatever the need for skin or throat beds or whatever the need to adjust St. Mary's undertakings the needs of the mothers and children in the area should be the first consideration. Were this, in fact, the case this decision would never have been contemplated, nor would such an injustice take place. It is only to be hoped that the authorities interested in child health and the treatment of sick children are aware of what is happening and are quick enough and interested and influential enough to prevent this tragic blunder occurring. Renowned as it is, St. Mary's Hospital stands only to lose by this proposal, not only in reputation but by additional strain on its resources. It is to be hoped that those responsible will think again and be prepared to do the just thing.—I am, etc.,

London, W.C.1. RODERICK MAGGS.

What is Social Medicine?

SIR,—I am much obliged to Professor W. Hobson for his very lucid and interesting letter (September 3, p. 546) in reply to my previous letter, and also to Dr. Alice M. Stewart for her courteous letter supporting the views of Professor Hobson. Both writers make it quite clear what they understand by the term social medicine, and no one could gainsay the importance of the work which they envisage, and in which they are engaged. But why call it social medicine? Is not all medicine social, at least in its practical application? And is not social medicine, as explained in these two letters, just preventive medicine writ large? There can only be one purpose animating both—

namely, the promotion of health and the prevention of disease. Social medicine may seek to study and evaluate the conditions, social or otherwise, affecting the incidence of diseases which have not hitherto been investigated on comprehensive lines, and may be able to do so with more efficient means of research than the old public health could afford; but surely this is only a natural extension of the principles of the old preventive medicine, which never set any bounds to its sphere of work.

Public health work in the past sought primarily to provide healthy conditions of life, and by means of health education to secure the intelligent co-operation of the public. Then it made direct attacks on those diseases which appeared most amenable to prevention, e.g., tuberculosis, enteric fever, diphtheria, and venereal diseases, and has done so with a large measure of success. But it did not consider its sphere limited to infectious disease, and by embarking on its schemes for maternity and child welfare, and the school medical service, it entered the realm of general medicine, though mainly from the preventive point of view. Even juvenile delinquency, mentioned by Professor Hobson, has not been overlooked at our child-guidance clinics.

I must confess on re-reading this letter that I may have been engaged on a petty hair-splitting crusade, but I did want to show that the old public health, as it is now called, was not such a hidebound affair as some people seem to think, and that the new public health is not so new as some people try to make out.—I am, etc.,

Torquay. THOMAS GIBSON.

Conceptions of Right and Wrong

SIR,—I can hardly congratulate Dr. J. E. Wilson (September 24, p. 711) on making an allegedly confused opinion of mine on the M'Naghten rules any clearer. With due respect, he seems to have bemused himself with legal terminology and, so far as I can understand his words, manages by a solemn blending of verbal incompatibles to indicate that the answer is in the affirmative and also in the negative.

A simple question was asked in my previous letter about the meaning of the word "wrong" in the M'Naghten rules (used for brevity and convenience—I know about the answers of the judges, etc., which Dr. Wilson brings up). I repeat the question in the plainest way I can think of: (*a*) Does the word "wrong" (as used in the M'Naghten rules) mean wrong according to English law? (*b*) Does it mean morally wrong? (*c*) Is it capable of meaning both according as it suits the purpose of counsel? If Dr. Wilson can cease being awed by the fact that he is dealing with the law and, in equally plain and simple language (preferably in terms of "yes" and "no"), will give me the authoritative answer I am seeking, I shall be in his debt. I might add that I am not in any way abashed by Latin tags.—I am, etc.,

London, W.1. FREDERICK DILLON.

The M.R.C.P.

SIR,—May I draw your attention to the manner in which the Royal College of Physicians introduced the recent changes in the Membership examination? The new regulations were first published at the end of July. The changes which they involved, particularly the new rule forbidding entry to those who have been qualified less than 18 months, were to take effect in the next examination, held at the end of September. However necessary the changes may have been it was surely discourteous of the Royal College to make these sweeping reforms without notice. No university authority would consider a similar change, even in its qualifying examinations, without at least six months' warning being given. The conflicting claims of national service and Membership make it even more difficult for the postgraduate to adjust his plans to such abrupt pronouncements.

To make matters worse, the secretarial staff of the College had no information concerning the details of the 18 months' restriction (i.e., that the period was to be measured from the date of registration to a date one month before the start of the examination) until the week ending September 3. It was possible, therefore, for a candidate who had thought himself just eligible for the September examination to be refused admission less than one month before the date of the first papers. Six months spent in polishing up is largely wasted when a sudden decision of the Royal College puts the examination into the dim period which lies beyond 18 months of military service. —I am, etc.,

HOUSE-PHYSICIAN.

Myxoedematous Madness

SIR,—Dr. E. B. Davies (September 24, p. 706) writes that I inferred that the pattern of psychotic disorder was determined by myxoedema and thinks the title of my paper, "Myxoedematous Madness" (September 10, p. 555), suggests that a specific type of psychosis exists. That is the opposite of what I said—e.g., "Certainly in the series I have observed there has been no constant type of psychosis. . . . It is the disease which is the characteristic feature, not its mental manifestations. . . . There is no specific psychosis." By the title "Myxoedematous Madness" I meant that the myxoedema caused the madness. For instance, the expression "hypoglycaemic reaction" implies that hypoglycaemia causes the reaction, but does not imply that all hypoglycaemic patients behave in a similar way (which they certainly do not).

Dr. Davies suggests that in my cases the myxoedema and the mental symptoms were a coincidence, and considers it misleading to call the association an organic psychosis. It seems fairly obvious the psychoses were organic for several reasons: (1) Because the onset of the psychosis was in every case after the onset of myxoedema. If the association were fortuitous it would be likely for some of the cases to have had psychotic symptoms first. (2) Because the majority recovered dramatically with thyroid. (3) Because in the case that stopped thyroid the mental symptoms returned. (4) Because 50% of cases of myxoedema seen have had psychotic symptoms, whereas 50% of women between 30 and 50 are not psychotic as far as I have noticed. (I have charge of an endocrine clinic and two general medical wards as well as a mental observation ward.)

Dr. Davies's attitude that the search for organic causes for psychoses is as fruitless as the search for the philosopher's stone is not a helpful one. Surely the "gold of psychopathology" is less helpful than malaria in a case of G.P.I. Many organic conditions—cerebral tumour, neurosyphilis, pneumonia, hypoglycaemia, and so forth—undeniably cause psychoses which appropriate treatment usually cures. I never wrote (as Dr. Davies seems to think) that "all the common psychoses . . . are determined by organic causes." I suggested that *some* might be found to be so caused. The majority of psychoses remain of unknown or psychopathological origin, but where physical causes exist their detection is a rewarding task for either physician or psychiatrist.—I am, etc.,

London, N.W.10. RICHARD ASHER.

POINTS FROM LETTERS

Distinction Awards

Dr. A. B. STEWART (Bury, Lancs) writes: Patients have already decided which family doctor will help them most and have awarded him their capitation fees. There is no chance of distinction awards for G.P.s. In my opinion the primary duty of the consultant is to help, in every sense of the word, the family doctor and through him the patient. If this opinion is accepted it follows that the G.P. should decide which consultants have given most assistance and thus qualify for distinction awards. Logically this process for deciding distinction awards can be carried a further stage. Consultants whose distinction awards are decided by G P.s should in turn decide which of their colleagues outside the orbit of G.P.s are rendering most help in the assistance given to family doctors and their patients, thus qualifying for distinction awards. Thus the sequence of reward and responsibility, from patient to remotest research worker, could be made complete.

Medical Notes in Parliament

Imported Books

During the special sittings of Parliament Mr. HAROLD WILSON made a statement on September 29 in the House of Commons about the relaxation of import restrictions. He announced the issue, as from October 5, of open general licences which would permit anyone to import the goods concerned without an import licence from any country other than those specifically excluded. He circulated a list of goods to be included on open general licences, which specified chemicals, drugs, and medicines, with various medical, surgical, and dental appliances and instruments. Books were also on the list; and from October 5 an open general licence would be issued for all imports of books from "soft currency" countries. Countries excepted from the scope of open general licences include the United States, Canada, countries in Central and South America, Belgium, Switzerland, Western Germany, the U.S.S.R., and European countries associated with it. On September 27 Mr. M. C. HOLLIS had raised the question of the licensing of the import of books. He said that as a result of this licensing the country's educational life had suffered. Frequently pupils had been told to read for examinations books which were not obtainable in this country. Scientific work had been hampered. Since by the loan agreement Britain must not discriminate against the Americans, it must exclude all works from every country so that the Americans did not have a grievance. If they could not have unlicensed import of books from the United States of America, at least they should have a free import of books from Europe, Eire, and the Dominions.

Mr. KENNETH LINDSAY said almost every country represented at the Strasbourg Assembly had similar quotas and restrictions to Great Britain. European unity should be made a reality at least in the world of books.

Mr. A. G. BOTTOMLEY, replying for the Government, said that as a result of the Anglo-American Loan Agreement they could not allow books to come into this country which they prohibited from the United States. Learned scientific and technical books were allowed in at the rate of 200% by value of pre-war imports. Import licences were issued quarterly, and the Government was arranging that for the next quarter the same ratio as before would come in. In addition, by the open general licence scheme any student who required a certain book could get it, although in some cases delay was unavoidable. The import of books from the United States must be limited. The Government could not consider taking anything further from the United States.

Medico-Legal

DRUGS LEFT IN CAR

A doctor was recently fined £10 for keeping dangerous drugs other than in a locked receptacle.[1] He had pleaded guilty. The prosecution contended[2] that the doctor's case had been found with some of its contents strewn on the ground. The case was taken to the police and was found to be unlocked. There was no sign of the lock having been tampered with. Among the contents missing were some tablets of pethidine and some morphine preparations.

The defence said that all the drugs were recovered immediately and no harm had been caused to anybody. The only person who could report the loss of dangerous drugs from a doctor's car was the doctor himself. If doctors were to be rewarded for reporting their loss to the police by being prosecuted, they would be discouraged from reporting it. The magistrate said that a serious case had been aggravated by the doctor leaving the unsecured drug case in his unlocked car.

[1] *Bristol Evening World*, July 12.
[2] *Bristol Evening Post*, July 12.

Universities and Colleges

UNIVERSITY OF ABERDEEN

At a medical graduation ceremony on September 28 the following degrees were conferred:

M.D.—*G. S. Riddell, W. F. Russell.

M.B., Ch.B.—*W. I. Cranston, †J. G. Henderson, †G. G. Mathieson, †W. W. Wilson, B. C. Abernethy, Isobel B. Alexander, J. Barron, A. A. W. Boyd, Katharine McE. Brodie (née Le Roux), Margaret McG. Chrystall, F. Clark, I. McI. Cochran, W. Cochran, I. A. Cook, F. T. Crossling, H. J. Crow, G. MacG. Davidson, Jean L. Davidson, Kathleen M. Dawson, B. W. Duthie, E. A. Fox, A. B. Fraser, D. E. Fraser, D. MacL. Fraser, Doreen M. M. Gove, R. B. Gove, A. Hird, J. D. Hunter, J. C. S. Jeffrey, Jean D. Jockel (née Troup), F. F. Kinnaird, J. Knowles, I. H. Lewis, A. Lorimer, A. McK. McGregor, J. A. McGregor, Yvonne M. H. McGregor, Mairi E. Macleod, D. K. McTaggart, W. G. C. Manson, A. T. Mennie, R. S. W. Middleton, C. Miller, Frances F. Milne, G. A. W. Milner, R. W. Milner, N. Murray, W. D. Nicholson, Helen R. Phemister, J. W. Price, P. E. Rixon, J. Rose, Catherine I. M. Ross, R. G. Ross, W. A. Ross, G. S. Selbie, R. McK. Sinclair, R. A. Smith, Eileen M. Spence, Doris L. Stephen, G. S. Stirling, Isobel R. S. Troup, R. G. Troup, Margaret F. Tweddle, D. C. Watler, G. L. Watt, Kathleen M. Watt, A. A. Will, G. A. Wood, Constance M. Yule (née Pole), R. M. Yule.

*With honours. †With commendation.

UNIVERSITY OF LONDON

A course of three lectures on "The Chemistry of the Transuranics and Other Newly Discovered Elements" will be given by Professor H. J. Emeléus, F.R.S., at the University College (Chemistry Theatre), Gower Street, London, W.C., on Mondays, October 31, November 7 and 14, at 5.15 p.m.

Mr. A. J. Wright, Director of Medical Postgraduate Studies in the University of Bristol, will deliver the Semon Lecture on "Tonsillar Function: A Review of the Evidence" at the Royal Society of Medicine, 1, Wimpole Street, London, W., on Thursday, November 3, at 5 p.m.

Professor J. Z. Young will deliver two lectures on "The Structure of Peripheral Nerve" at University College, Gower Street, London, W.C., on Mondays, October 10 and 17, at 5.15 p.m.

A course of three lectures on "Growth and Reproduction of Bacteria" will be delivered by Sir Paul Fildes, F.R.S., in the Anatomy Theatre of University College, Gower Street, W.C., on October 19, 20, and 21, at 5.30 p.m.

Sir James Learmonth, Professor of Surgery and Clinical Surgery in the University of Edinburgh, will deliver a course of four Heath Clark Lectures at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, W.C., on November 21, 22, 23, and 24, at 6 p.m. His subject is "The Contribution of Surgery to Preventive Medicine."

All the above lectures are addressed to students of the University and to others interested in the subjects. Admission is free, without ticket.

UNIVERSITY OF WALES

The Council of the Welsh National School of Medicine has appointed Frederick Roland George Heaf to the David Davies Professorship of Tuberculosis at the school.

Dr. Heaf qualified at St. Thomas's Hospital in 1918, taking the Cambridge degree two years later. He proceeded M.D. in 1923 and was elected F.R.C.P. in 1946, having taken the Membership in 1941. Dr. Heaf is Senior Medical Officer, London County Council, Adviser in Tuberculosis to the Ministry of Health, and president of the British Tuberculosis Association.

UNIVERSITY OF LIVERPOOL

The following candidates have been approved at the examination indicated:

FINAL M.B., Ch.B.—*Part I:* Hilary A. Hagan, J. A. Howe, W. R. Howell, H. G. McDonald, Angela M. M. Manning, T. W. Merrick, J. B. Newton, E. Patrick, J. W. Prout, Megan Roberts, D. Winter.

UNIVERSITY OF SHEFFIELD

The following candidates have been approved at the examinations indicated:

M.D.—Helen N. Mellanby, E. L. M. Millar.

FINAL M.B., Ch.B.—Daphne Burkinshaw, Nancy Cole, J. D. Crabtree, P. Kelly, Barbara Kilpatrick, P. O. M. McGirr, S. Mohamedi, F. L. Myers, G. H. Pagdin, Kathleen Sampson.

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended September 17. [No. 37

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1949					1948 (Corresponding Week)				
	(a)	(b)	(c)	(d)	(e)	(a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	34	2	25	4	—	26	2	11	—	—
Deaths		—	—				—	—		
Diphtheria	78	10	30	6	5	126	12	34	6	2
Deaths	1	—	—	—	—	3	2	1	—	—
Dysentery	86	7	54	1	2	50	5	39	—	—
Deaths				—	—				—	—
Encephalitis lethargica, acute	1	—	—	—	—	1	—	—	—	—
Deaths		—					—			
Erysipelas			27	2	1			35	6	3
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				142					58	
Deaths	27	—	11	16	4	36	3	6	2	1
Measles*	688	42	40	48	40	2,614	83	45	11	39
Deaths†			1	1	—			—	—	—
Ophthalmia neonatorum	54	12	6	—	—	47	9	14	—	—
Deaths										
Paratyphoid fever	18	1	5 (B)	2 (B)	—	17	2	—	—	—
Deaths	—	—	—	—	—	—	—	—	—	—
Pneumonia, influenzal	211	10	2	1	2	283	9	3	2	4
Deaths (from influenza)‡	6	—	—	—	—	4	1	—	—	—
Pneumonia, primary			85	10				136	16	
Deaths	116	18		9	3	108	10		5	3
Polio-encephalitis, acute	31	3				2	—			
Deaths										
Poliomyelitis, acute	311	38	8	3	3	72	6	2	2	—
Deaths§	20	2				4	—			
Puerperal fever		—	10				—	17		—
Deaths										
Puerperal pyrexia‖	118	9	4	—	2	101	9	4	—	—
Deaths		—					—			
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	942	75	132	62	96	925	62	220	91	49
Deaths†			—	—	—			1	—	—
Smallpox	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	4	1	1	2	—	28	—	5	2	—
Deaths	—	—	—	—	—	—	—	—	—	—
Typhus fever	4	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	1,180	48	75	33	45	2,635	166	68	49	10
Deaths	1	—	—	—	—	12	2	—	1	—
Deaths (0–1 year)	225	26	49	36	15	268	33	37	14	8
Deaths (excluding stillbirths)	3,702	567	482	162	88	3,860	601	506	159	95
Annual death rate (per 1,000 persons living)			9·7	10·0				10·2	9·9	
Live births	7,099	1098	891	373	225	7,332	1194	882	427	212
Annual rate per 1,000 persons living			17·9	23·1				17·8	26·7	
Stillbirths	188	17	27			203	24	29		
Rate per 1,000 total births (including stillborn)			29					32		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

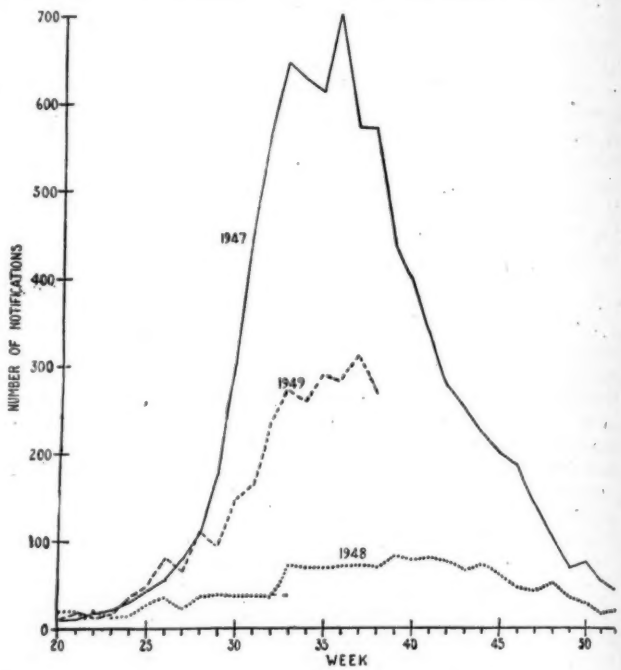
§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

EPIDEMIOLOGICAL NOTES

Poliomyelitis

Notifications in England and Wales for the week ended September 24 were: poliomyelitis 268 (311), polio-encephalitis 27 (31). The figures for the previous week are shown in parentheses. This is the first substantial fall since the rise in notifications began in the twenty-fourth week of this year. The curve generally has followed that of 1947 fairly closely, and it is to



be hoped that the decline which began in the thirty-seventh week of that year has now set in. For comparison the curves for the present year and for 1948 and 1947 are set out in the accompanying graph.

Multiple cases (poliomyelitis and polio-encephalitis together) were reported from the following counties: London 48 (41), Berkshire 3 (7), Cheshire 7 (4), Cornwall 8 (10), Devon 5 (5), Dorset 4 (3), Essex 17 (18), Hertford 7 (4), Kent 18 (16), Lancaster 24 (29), Leicester 5 (13), Lincolnshire, Holland 4 (1), Lincolnshire, Lindsey 4 (6), Middlesex 20 (25), Norfolk 2 (3), Northampton 4 (3), Northumberland 13 (10), Nottingham 9 (11), Oxford 3 (0), Soke of Peterborough 2 (1), Somerset 7 (8), Southampton 8 (10), Suffolk East 5 (1), Surrey 11 (14), Sussex West 2 (1), Warwick 8 (10), Westmorland 2 (0), Wiltshire 9 (6), Yorks West Riding 19 (33), Glamorgan 3 (3).

In the United States a peak of incidence was reached with 3,419 cases of poliomyelitis in the week ended August 20, and since then the notifications have been fewer. Already 29,051 cases have been reported this year.

Sex and Age Composition of Population

Estimates compiled by the Registrar-General of the civilian populations of each local government area in England and Wales, showing the numbers of each sex at various age groups, have recently been published.[1] Figures such as these are usually only available when a census is taken. Owing to the war, there has been no census since 1931, and the latest figures previously available were those based on the enumeration carried out for national registration purposes on September 29, 1939. Those figures were affected by mobilization and evacuation and could not be regarded as reflecting normal conditions.

The present figures relate to December 31, 1947, and have been largely based on a special examination of the individual

[1] *Estimates of the Sex and Age Distribution of the Civilian Population in Regions and Administrative Areas of England and Wales at December 31, 1947.* H.M.S.O., price 2s. 6d.

population records maintained in the local National Registration Offices through the country. In most areas there are wide differences between the numbers of men and numbers of women at certain age groups, which are mainly due to the exclusion of members of the armed Forces and merchant seamen from the figures. For the country as a whole the approximate ratios of males to every 1,000 females (*including* members of the armed Forces and merchant seamen) at the age groups mainly affected are as follows:

All ages	940		25–34		986
18–19	1,017		35–44		992
20–24	1,021		45–54		988

Comparing the 1947 figures with those obtained from the 1931 census, the general ageing of the population is readily apparent. For instance, during this 16-year period (*a*) the proportion of the total population of England and Wales under 15 years of age has fallen from 23.8% to 21.9%, and the proportion over 65 has risen from 7.4% to 10.9%; (*b*) corresponding figures for Wales alone are: under 15, a fall from 26.6% to 22.4%; over 65, a rise from 6.7% to 10.8%; (*c*) for the administrative county of London the figures are: under 15, a fall from 21.5% to 18.9%; over 65, a rise from 7.3% to 10.8%.

Discussion of Table

In *England and Wales* there were increases in the notifications of scarlet fever 213, acute poliomyelitis 27, dysentery 27, and diphtheria 12, with decreases in the incidence of measles 187 and whooping-cough 48

An increased incidence of scarlet fever was reported throughout the country. The rise in the incidence of diphtheria was due to scattered isolated cases; the largest returns during the week were London 10, Durham 10, and Lancashire 9. The largest returns for measles came from Lancashire 106, Durham 72, London 42, and Yorkshire West Riding 38. The largest fluctuation in the incidence of whooping-cough was an increase of 31 in Middlesex.

Outbreaks of dysentery were notified in Durham, Hetton U.D. 15; Glamorganshire, Neath M.B. 11; Yorkshire West Riding, Dewsbury C.B. 8; and Essex, Thurrock U.D. 6. The incidence of food-poisoning was high in Essex 86, London 40, and Norfolk 28.

In *Scotland* there were decreases in the notifications of dysentery 38 and acute primary pneumonia 24, while increases were reported for cerebrospinal fever 13, whooping-cough 13, and diphtheria 9. The rise in the incidence of cerebrospinal fever and diphtheria was mainly contributed by Glasgow. Of the 54 cases of dysentery 45 were notified in Glasgow. Cases of paratyphoid fever were notified from Lanark County 3 and Glasgow 2.

In *Eire* there were falls in the notifications of whooping-cough 54 and scarlet fever 26, with a rise in the incidence of measles 26. Notifications of diarrhoea and enteritis were 3 more than in the preceding week, but in Dublin C.B. the notifications fell from 115 to 105. The decrease in the incidence of whooping-cough and scarlet fever was due to the experience of Dublin C.B. A small rise in the incidence of measles was recorded throughout the country.

In *Northern Ireland* the chief fluctuations were a rise of 27 in the notifications of scarlet fever and a decrease of 26 in the notifications of whooping-cough.

Week Ending September 24

Notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,097, whooping-cough 1,061, diphtheria 92, measles 659, acute pneumonia 226, cerebrospinal fever 35, acute poliomyelitis 268, acute polio-encephalitis 27, dysentery 78, paratyphoid fever 23, typhoid fever 8, food-poisoning 245.

The Ministry of Food states that minute traces of lead in curry powder and copper in tomato products are not uncommonly found. Maximum limits for these elements have therefore been prescribed, and the composition of these and other commodities defined, by the Food Standards (Curry Powder) Order, 1949, and the Food Standards (Tomato Ketchup) Order, 1949, under the Defence (Sale of Food) Regulations.

Medical News

Hospital to Reopen

The South-Eastern Hospital for infectious diseases at New Cross, London, S.E., is to be reopened as the New Cross General Hospital, with accommodation for about 200 patients.

"Academician Pavlov"

As part of the Pavlov centenary celebrations the film "Academician Pavlov" was shown to an invited audience on September 26. The film, which runs for over an hour, was well received.

Jodrell Chair of Physiology

Professor C. Lovatt Evans, F.R.S., has retired from the Jodrell Chair of Physiology of London University, and was succeeded from October 1 by Professor George Lindor Brown, F.R.S., whose appointment has been announced previously.

Streptomycin Manufacture Controlled

From October 1 streptomycin can be manufactured for sale only under licence, and it must conform with prescribed conditions as to strength, quality, and purity. These requirements are laid down in the Therapeutic Substances Amendment Regulations, 1949.

Import Restrictions Relaxed

The Board of Trade has announced that restrictions have been relaxed on the import of drugs and other chemicals, medical and surgical instruments, and books obtained from countries where they can be bought without risk of losing gold or dollars.

Prize for Work on Thyroid

The American Goiter Association offers the Van Meter prize of 300 dollars and two honourable mentions for the best essays submitted on original work related to the thyroid gland. The essays may be on either clinical investigation or research, and should not be longer than 3,000 words. Two copies should be sent to the corresponding secretary, Dr. George C. Shivers, 100, East St. Vrain Street, Colorado Springs, Colorado, U.S.A., before January 15, 1950.

Colour Television

A demonstration of colour television, with equipment suitable for viewing surgical operations, was given by Messrs. Pye, Ltd., at Olympia on October 3. A number of articles were shown being televised—some, brightly coloured, such as a bowl of flowers, and others, such as human bones, less colourful. The equipment operates at 405 lines a frame, and gives the same definition as the B.B.C. transmissions. The colours are effectively natural, though comparison with the objects being televised showed that they departed considerably from their actual colours. There was no flare from the highly polished surgical instruments, and the depth of focus allowed the furthest parts of a mandible to be seen as clearly as the nearest when it filled the screen. The apparatus seems to be entirely suitable for televising operations, and probably an audience of 20 or 30 would have a good view of the surgical field. At present the approximate cost of the equipment is £25,000.

Wills

Dr. John Wardle Bone, formerly Treasurer of the B.M.A., left £73,952; Dr. Joseph Henry Churchill, of Bath, left £12,369; Dr. Charles Cromhall Easterbrook, of Edinburgh, £48,949; Dr. Wilfred Nightingale, of Lytham St. Annes, £13,131; Dr. John Finlayson Lang, of Rathgate, West Lothian, £12,560.

COMING EVENTS

Royal Eye Hospital Lectures

A series of lectures at the Royal Eye Hospital, St. George's Circus, London, S.E., opened on October 3 and will be continued during this month and in November and December, and January, 1950. The lectures are open to both postgraduate and undergraduate students. Details of fees and subjects may be obtained from the secretary of the hospital.

Nurses' Conference

The eighth conference on the nation's nurses, arranged by the Royal College of Nursing (Henrietta Place, Cavendish Square, London, W.), will be held at the College to-day and to-morrow (Friday and Saturday, October 7 and 8) at 10 a.m. The subject for discussion on October 7 is "The Industrial Nursing Service and the Worker," and that on October 8 "Economy in Nurse Power." The conference fee is £1 1s.

Royal College of Obstetricians and Gynaecologists

The annual dinner of the Royal College of Obstetricians and Gynaecologists will be held at Dorchester Hotel, Park Lane, London, W., on Wednesday, October 12, at 7 for 7.30 p.m.

Adlerian Society of G.B.

The first meeting of the medical section of the Adlerian Society of Great Britain will be held at 11, Chandos Street, Cavendish Square, London, W., on Thursday, October 13, at 8 p.m. Papers will be read by Drs. Neville Murray and Joshua Bierer on "Prolonged Sneezing as a Psychosomatic Symptom." The discussion will be opened by Mr. E. O. Harris and Drs. C. J. C. Britton and H. Fleetwood Walker. All medical practitioners interested are invited, and further information may be obtained from Dr. Christine E. Cooper, honorary secretary of the medical section, 115 Langford Court, London, N.W.8.

Nurses and Midwives Conference

The 34th annual Professional Nurses and Midwives Conference will be held, under the auspices of the *Nursing Mirror*, at Seymour Hall, Seymour Place, London, W., from October 17 to 21, under the presidency of Viscount Addison. The programme is as follows: October 17, 11 a.m., opening address; 11.45 a.m., Dr. C. T. Potter, "Neonatal Period and Its Disorders"; 2.45 p.m., Sir William Gilliatt, "Changes in the Practice of Obstetrics"; 4.45 p.m., Mr. H. G. E. Arthure, "The Management of the Puerperium." October 18, 10.15 a.m., Professor A. M. Boyd, "Some Recent Advances in Surgery of the Blood Vessels"; 11.30 a.m., Mr. T. Holmes Sellors, "The Blue Baby—Operation for Congenital Heart Disease"; 2.15 p.m., Mr. D. W. C. Northfield, "Sympathectomy"; 3.30 p.m., Mr. G. A. Mason, "Surgical Treatment of Coronary Thrombosis"; 4.45 p.m., Mr. Wylie McKissock, "Operations for Changing the Mental State." October 19, 10.15 a.m., Mr. Terence E. Cawthorne, "Ménière's Disease"; 11.30 a.m., Dr. C. F. Terence East, "Hypertension"; 2.15 p.m., Dr. H. S. Le Marquand, "Endocrine Disorders of Childhood"; 3.30 p.m., Dr. J. B. Murray, "Psychosomatic Medicine"; 4.45 p.m., Mr. R. W. Knowlton, "Diagnosis and Treatment of Non-venereal Vaginal Discharges." October 20, 10.15 a.m., Mr. George Wynn-Williams, "Hyperemesis Gravidarum"; 11.30 a.m., Mr. Arthur C. H. Bell, "Albuminuria of Pregnancy"; 2.15 p.m., Mrs. Fox, "Relaxation in Childbirth"; 3.30 p.m., Mr. F. W. Roques, "Displacement of the Uterus"; 4.45 p.m., Professor R. J. Kellar, "Rupture of the Uterus." October 21, 10.15 a.m., Dr. Alfred Piney, "Bone Marrow Biopsy"; 11.15 a.m., Professor J. S. Mitchell, "Radioactive Isotopes"; 12.15 p.m., Dr. F. C. O. Valentine, "Streptomycin and the Newer Antibiotics"; 2.30 p.m., Mr. Leon Gillis, "Recent Progress in the Treatment of Arm Amputations and Arm Prostheses." Throughout the week there will be twice-daily sessions of the latest medical films, and in the exhibition hall there will be a display of drugs, foods, pharmaceuticals, and equipment. Admission to the conference and exhibition is limited to professional visitors. Applications for tickets should be made to matrons of hospitals and similar institutions, to nursing associations, to the Royal College of Midwives, or to the organizer of the conference, Dorset House, Stamford Street, London, S.E.1.

Osler Club

The next meeting of the Osler Club will take place on Friday, October 21, at 8 p.m., in the Wellcome Historical Medical Library, 183, Euston Road, London, N.W.1. The speakers will be Mr. W. R. LeFanu, librarian of the Royal College of Surgeons, on "Edward Jenner, Author and Letter Writer," and Professor G. S. Wilson, of the Ministry of Health Public Health Laboratories, whose subject will be "Smallpox and After." There will also be an exhibition of books and papers related to Edward Jenner and his work.

American Public Health Association

The 77th annual meeting of the American Public Health Association will be held in New York on October 24–28.

27 General Hospital

A reunion dinner of No. 27 General Hospital will be held at the Eccleston Hotel, Eccleston Square, London, S.W.1, on Saturday, October 29, at 6.30 for 7.15 p.m. (dress informal). Remittances of 15s. 6d. (inclusive) should be sent to Mr. G. L. Pudney, 161, Silverleigh Road, Thornton Heath, Surrey.

Brigade Surgeons' Conference and Dinner

The surgeons of the St. John Ambulance Brigade will hold their annual conference and dinner at the Waldorf Hotel, Aldwych, London, W.C., on Saturday and Sunday, October 29 and 30, when Lord Horder will be the principal guest at the dinner. At the conference there will be talks on the effects of atomic warfare and the treatment of casualties; on shock, its effects and treatment; and on the use of films in teaching. Further details can be obtained from the Surgeon-in-Chief, St. John Ambulance Brigade, 8, Grosvenor Crescent, London, S.W.1.

Royal Institute of Philosophy

The programme for the 1949–50 session of the Royal Institute of Philosophy includes lectures to be given at University Hall, 14, Gordon Square, London, W.C., and evening meetings to be held at University College (Anatomy Theatre), Gower Street, London, W.C., during this month and in November and January, February, and March, all of which are open to the public. Cards of admission may be obtained free of charge from the director of studies of the Institute at 14, Gordon Square, W.C.1. Details will be published under "Societies and Lectures" in the *Journal* week by week.

Canadian Course in Cytology

A course in clinical cytology for the diagnosis of uterine and other types of cancer will be held at McGill University, Montreal, under Dr. J. Ernest Ayre, on November 7–21, at the Cytological Laboratories, Royal Victoria Hospital, Montreal. The fee for tuition is $100.

Courses in Psychiatry

The University of London Institute of Psychiatry will hold courses for first-year and second-year students on psychology and psychiatry this autumn. The fee for one term's lectures is 12 guineas, and for separate series of lectures proportionate fees will be charged. Particulars may be obtained from the dean, Institute of Psychiatry, Maudsley Hospital, Denmark Hill, London, S.E.5 (Telephone: Rodney 2634).

SOCIETIES AND LECTURES

Friday

National Hospital, Queen Square, London, W.C.—October 7, 5 p.m., "*Observations on the Anatomy of Memory*," by Dr. Wilder Penfield (Montreal).

Monday

London University.—At University College, Gower Street, London, W.C., October 10, 5.15 p.m., "*The Structure of Peripheral Nerve*," by Professor J. Z. Young.

Medical Society of London, 11, Chandos Street, Cavendish Square, London, W.—October 10, 8.30 p.m., General meeting; 8.45 p.m., "*The Sigmoidoscope*," Presidential Address by Mr. Lionel E. C. Norbury.

National Hospital, Queen Square, London, W.C.—October 10, 5 p.m., "*Allergic Manifestations in the Nervous System*," by Dr. Foster Kennedy (New York).

Tuesday

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—October 11, 5 p.m., *"Histology of the Skin,"* by Dr. I. Muende.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Postgraduate Medical School of London, Ducane Road, W., October 11, 3 p.m., *"Problems of Infertility in a County Centre,"* by Dr. Margaret Jackson.

SOCIETY OF CHEMICAL INDUSTRY: FINE CHEMICALS GROUP.—At Royal Institution, Albemarle Street, London, W., October 11, 7 p.m., *"Biological Polymerization with Special Reference to Polysaccharide Synthesis,"* by Professor M. Stacey, Ph.D., D.Sc.

Wednesday

GLASGOW UNIVERSITY: DEPARTMENT OF OPHTHALMOLOGY.—October 12, 8 p.m., *"Control of Clotting in Ophthalmology,"* by Dr. W. O. G. Taylor.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS, 58, Queen Anne Street, London, W.—October 12, 2.30 p.m., *"Scotland's Contribution to the Progress of Midwifery in the Eighteenth and Early Nineteenth Centuries,"* William Meredith Fletcher Shaw Memorial Lecture by Professor R. W. Johnstone.

SOCIETY OF CHEMICAL INDUSTRY: FOOD GROUP.—At Medical Society of London, 11, Chandos Street, Cavendish Square, London, W, October 12, 6.15 p.m., meeting of Microbiological Panel. *"Aspects of the Mineral Metabolism of Micro-organisms"* (1) *Use of Aspergillus niger for the Determination of Mineral Nutrients in Soil,* by Dr. D. J. D. Nicholas; (2) *Effect of Ion Exchange Treatment on (a) Composition, (b) Microbiological Stability of Apple Juice,* by Drs. D. W. Challinor and A. Pollard.

YORK MEDICAL SOCIETY.—At Tempest Anderson Hall, York, October 12, 3 p.m., *"New Pathways in Medicine,"* by Sir Henry Cohen.

Thursday

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—October 13, 5 p.m., *"Skin Affections of the Hands and Feet,"* by Dr. G. B. Mitchell-Heggs.

NATIONAL HOSPITAL, Queen Square, London, W.C.—October 13, 5 p.m., *"Diagnostic Errors in Neurological Practice,"* by Professor G. H. Monrad-Krohn (Oslo).

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—October 13, 4.30 p.m., lecture-demonstration: *"Psychiatry,"* by Dr. D. Curran.

WESTMINSTER HOSPITAL SCHOOL OF MEDICINE, Meyerstein Lecture Theatre, Horseferry Road, London, S.W.—October 13, 5.30 p.m., Clinico-pathological demonstration. Discussion: *"Leukaemia and its Treatment."*

Friday

ROYAL INSTITUTE OF PHILOSOPHY, 14, Gordon Square, London, W.C. —October 14, 5.15 p.m., *"Scope and Aims of 'Synoptic' Philosophy,"* by Professor H. H. Price.

ROYAL SANITARY INSTITUTE.—At Tunbridge Wells Town Hall, October 14, 10 a.m., *"Newer Methods in the Tracing of Typhoid Outbreaks Including the Value of Phage Typing,"* discussion to be opened by Professor J. C. Cruickshank.

Saturday

NORTH OF ENGLAND OTOLARYNGOLOGICAL SOCIETY.—At Harrogate and District General Hospital, Knaresborough Road, Harrogate, October 15, 2 p.m., Annual Meeting.

NUTRITION SOCIETY.—At Department of Pharmacology, Birmingham University, October 15, 1.15 p.m., *"Triglyceride Fats in Human Nutrition,"* by Professor A. C. Frazer, Drs. J. Elkes and J. M. French (Department of Pharmacology, Birmingham University), Professor T. P. Hilditch (Department of Industrial Chemistry, Liverpool University), and Professor P. Kraut (Berlin).

YORK MEDICAL SOCIETY.—At 17, Stonegate, York, October 15, 8.30 p.m., *"Diagnosis and Prevention of Whooping-cough,"* by Professor Robert Cruickshank.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Cole.—On September 17, 1949, at City and County Hospital, Londonderry, to Nancy (née Jones), S.R.N., wife of J. O. Y. Cole, M.D., D.M.R.E., a son—David Owen James

Hargrove.—On September 23, 1949, at the Hill Nursing Home, Reading, to Elizabeth (née Corbett-Lowe), wife of Dr. Peter Hargrove, a daughter—Gillian Dingwall.

Hopwood.—On September 20, 1949, at Kampala, Uganda, to Shirley (née Newman), wife of Dr. B. E. C. Hopwood, a brother for Penelope Ann—John Burton.

Lewes.—On September 24, 1949, at The Haven, Great Chesterford, to Daphne (née Wailes) and David Lewes, M.R.C.P., a daughter—Jane Christina.

Ronchetti.—On Septemoer 18, 1949, at Winchmore Hill, to Sylvia (née Helme), wife of Dr. John Ronchetti, a sister for John Kirkland.

MARRIAGES

Brearley—Hewitt.—On September 8, 1949, at Sandiway, Cheshire, Roger Brearley, M.B., F.R.C.S., to Joyce Mary Hewitt.

Webber—Hay.—On September 28, 1949, at St. Peter's Church, March, Cambs, George Edward Francis Webber (formerly of Buenos Aires and India) to Hilda Russell Hay, M.B., Ch.B., D.P.H., County Medical Officer, Isle of Ely.

Any Questions ?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Streptomycin during Pregnancy

Q.—*Is there any evidence that administration of streptomycin during pregnancy is likely to result in labyrinthine damage to the foetus?*

A.—The answer to this question is probably not yet known, because comparatively few women have received streptomycin during pregnancy. Moreover, streptomycin has been available for only a short time, and it will presumably be necessary to wait until children exposed to its influence *in utero* are 1½ to 2 years old before their auditory function can be assessed with any degree of certainty. Streptomycin can cross the placenta, and has been demonstrated in the foetal blood in amounts comparable to those in the maternal circulation, and also in liquor amnii in heavy concentration; toxic effects might therefore be expected. On the other hand, there is some evidence that damage to the auditory apparatus is a less common side-effect in children than in adults.

This problem would appear to be of considerable importance, and it is to be hoped that those who have experience of administering streptomycin to pregnant women will comment on the results to the foetus, if possible relating them to the period of pregnancy at which treatment was given.

Temperature and Pulse Rate in Phthisis

Q.—*Above what levels of oral temperature and resting pulse rate is activity indicated in a patient with pulmonary tuberculosis (a) when resting in bed and (b) when getting up?*

A.—The variations which can occur in the so-called normal temperature in health are greater than is generally realized. A diurnal variation of 3° F. (1.6° C.) is common, and the temperature range is at different levels in different individuals. Thus, one healthy subject may have a daily variation between 97.2° and 99.2° F. (36.2° and 37.3° C.), while another's may be between 95° and 98° F. (35° and 36.7° C.). These facts, which have been fully described recently by Samson Wright (*Journal,* April 9, 1949, p. 610), are of great importance when evaluating the temperature of a tuberculous patient. It is necessary first to estimate the normal range for the particular individual, since a rise to 99° F. (37.2° C.) in a patient with a high normal range may be of no significance, whereas it may indicate fever in a patient with a low normal range. In general, it may be said that a reading above 99.5° F. (37.5° C.) in a patient who is resting in bed probably indicates disease activity. The temperature must be taken at the same times each day, and these should not be after meals: the thermometer must always remain in the mouth for a full five minutes to obtain an accurate reading. Allowance must be made for the considerable variations in temperature which accompany the menstrual cycle in most women. Occasionally a patient who has been in bed for some time will have an evening temperature of about 100° F. (37.8° C.), and this will come down to a lower level when the patient starts to get up. Such a "bed temperature" is by no means uncommon. When the patient is up and about, other factors, such as variations in external temperature and muscular exercise, will alter the temperature range. A rise in temperature of 1° F. (0.55° C.) after exercise is not uncommon, but this should settle down after half an hour's rest.

The pulse rate is a less reliable guide. Usually it follows the temperature, but it is much more easily affected by nervousness. A persistent tachycardia should lead one to suspect activity of the disease; wide variations in the pulse rate are probably due to psychological causes. It must be stressed that both temperature and pulse rate are far inferior to serial radiography in assessing the progress of a case of pulmonary tuberculosis. *X* rays not infrequently reveal active disease in a patient who is afebrile.

Urethritis

Q.—*(a) What are the signs and symptoms of urethritis in the male due to Trichomonas vaginalis, and what treatment is indicated? (b) Are there any cases on record of urethritis caused by spermicidal contraceptives?*

A.—(*a*) The signs and symptoms of urethritis in the male due to *Trichomonas vaginalis* do not differ in any important respect from those due to various other forms of non-gonococcal urethritis, but it is probable that *T. vaginalis* more often causes a balanoposthitis or prostatitis than a simple urethritis. Rendering the urine alkaline is said to be effective in most cases, but a more reliable form of treatment consists in filling the urethra with powdered acetarsol in water or saline, holding it there for a few minutes, and milking it back as far as possible towards the posterior urethra.

(*b*) Most venereologists consider that various contraceptive chemicals are liable to cause urethritis, but it is obviously difficult to prove that they do so.

Intravenous or Intramuscular Heparin

Q.—*Disregarding speed of action, is heparin less efficacious when given intramuscularly than when given intravenously?*

A.—Heparin, being expensive, is usually given intravenously, but it is just as efficient when given intramuscularly, provided the dose is at least doubled—some say trebled or quadrupled. The precise comparable dose is still uncertain.

Rheumatoid Arthritis and Epilepsy

Q.—*Are any statistics available showing the coincidence of rheumatoid arthritis and epilepsy? In a small experience I have not encountered such a combination. If the coincidence of the two diseases is rare, might the recent discovery of "cortisone" be a pointer to the aetiology of epilepsy?*

A.—There appear to be no statistics showing the coincidence of rheumatoid arthritis and epilepsy, nor is the occurrence of rheumatoid arthritis recorded as being more or less frequent in epileptics than in the normal population. It would seem a somewhat far-fetched assumption, on the basis of these negative observations, that there may be a common aetiological factor. It is known, however, that "cortisone" (17-hydroxy-11-dehydrocorticosterone; compound E) will produce a well-marked euphoria in arthritics and others, and this fact has led certain psychiatrists to assume that it may perhaps prove of some value in nervous and psychiatric illness.

Effect of Pregnancy on Libido

Q.—*Is there any explanation for the fact that after their first pregnancy many young women experience a loss of sexual appetite and satisfaction? There has been no active distaste in two cases seen recently—merely an indifference where before there had been desire. Both are healthy young women with second children, and no physical cause can be found. Is the condition likely to ameliorate—one case is of three years' duration, the other of 18 months? Is there any treatment?*

A.—Reduced sex desire after pregnancy, especially the first pregnancy, is the experience of most women. The fact that a fundamental objective of coitus has been achieved, the awakening of mother love with some readjustment of the woman's affections, the extra work and anxiety associated with looking after the child, etc., all play their part. A local organic basis is most unlikely so far as sex desire is concerned, although an overstretched vagina might diminish satisfaction. These troubles, however, are usually only temporary and clear up as the period of nervous strain passes, as physical well-being returns, and as the baby grows independent. If loss of libido should persist, another factor—fear of pregnancy—should be kept in mind, and in such a case the appropriate treatment is advice on contraception. Explanation and reassurance may be all that is necessary in other cases. The wife should avoid getting overtired, and the husband should have patience and understanding.

NOTES AND COMMENTS

Toxic Effects of "Diparcol."—Dr. R. C. Meek (Birmingham) writes: In "Any Questions?" in a recent issue of the *Journal* (August 13, p. 398) an inquiry was made by a reader regarding the dangers of the drug "diparcol." In the reply it is stated that French workers reported a fatal case of agranulocytosis but considered this to be due to other drugs used at the same time. In view of the present extensive use of diparcol I think the following experience may be of interest. The patient, a married woman aged 58, had suffered from post-encephalitic parkinsonism since about 1935. On admission to hospital on May 18, 1949, she showed extreme rigidity of the face, neck, trunk, and all four limbs, and a rhythmic tremor of the hands. Diparcol was started on May 29, 1949, in a dosage of 50 mg. b.d. The dosage was steadily increased till July 15, 1949, by which date she was receiving 1 g. daily. On this dosage there was considerable relief of the rigidity and tremor. She was kept on 1 g. daily till July 28, 1949, when slight mental confusion developed; the dosage was reduced to 400 mg. daily. On August 4, while still on 400 mg. daily, she complained of a sore throat and general malaise. Examination showed a temperature of 99.5° F. (37.5° C.), a patch of exudate on one tonsil, and a few small boils on the trunk. Diparcol, which was the only drug she was receiving, was stopped and she was put on penicillin 50,000 units 3-hourly. A white cell count showed a total of 3,900 per c.mm. with only 4% granular cells; a throat swab showed a heavy mixed growth with a coagulase-positive staphylococcus predominating. On August 5, 1949, in spite of treatment (which by this time included pentose nucleotide) the temperature had risen to 103° F. (39.4° C.), and she now showed large patches of exudate covering both tonsils. She died on August 6, 1949. At necropsy it was seen that there were ulcers on the posterior part of the tongue in addition to those on the tonsils. The lungs were oedematous, and there was congestion of the bronchial mucosa but no evidence of bronchopneumonia. The liver showed cloudy swelling and the spleen was large and soft. The bone marrow was not grossly abnormal macroscopically. The microscopic appearance of the bone marrow was summed up by the pathologist: "The appearance is that of diminished formation or destruction of early forms of the granulocyte series."

Medical Treatment of Myopia.—Mr. A. Seymour Philps (London, W.) writes: I was surprised to read under "Any Questions?" (August 13, p. 398) the statement that medical treatment of myopia, such as the administration of calcium, is not now much used, and that in these days chief reliance is placed on ordering a full correction at as early an age as possible, and that the glasses should be worn all day long. I should have thought that this was the exact opposite of the facts. Glasses are pieces of glass which help the eyes to focus, and they are given to the child in order that he or she may see what is going on and derive some benefit from education. I thought it was commonly agreed that they had no influence whatever on checking myopia, and certainly it is true that myopes do not become worse by leaving them off. While proof is difficult, it does seem that attention to general health, feeding, conditions of work, and the possible administration of calcium and vitamin D do have some good effect in checking myopia, and I think it is a pity that a statement to the contrary should go unchallenged in the *Journal*.

Family Planning.—The General Secretary of the Family Planning Association writes: The quotations chosen by Dr. Clark (September 17, p. 656) from literature distributed by the Family Planning Association might lead readers to suppose that this association restricts its services to the classes of patients to whom he refers. I should like to point out that at all F.P.A. clinics (a list of which can be obtained from this office at 69, Eccleston Square, S.W.1, price 6d., post free) medical advice on contraception is available to all married women who attend. The F.P.A. would entirely agree with Dr. Clark's views that the size and spacing of the family is a matter to be decided by the parents who will have to take the responsibility of the welfare and upbringing of any children born to them.

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